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NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and  
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NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT  
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),  
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003  
NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS INTER General Internet Information  
NEWS LOGIN Welcome Banner and News Items  
NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
NEWS WWW CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 14:29:18 ON 26 MAY 2003

=> file reg

| COST IN U.S. DOLLARS | SINCE FILE<br>ENTRY | TOTAL<br>SESSION |
|----------------------|---------------------|------------------|
| FULL ESTIMATED COST  | 0.21                | 0.21             |

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STRUCTURE FILE UPDATES: 25 MAY 2003 HIGHEST RN 519753-05-0

DICTIONARY FILE UPDATES: 25 MAY 2003 HIGHEST RN 519753-05-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when  
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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNote 27, Searching Properties  
in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>

Uploading 09912163.1

Welcome to STN International! Enter x:x

LOGINID:sssptal611sxp

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

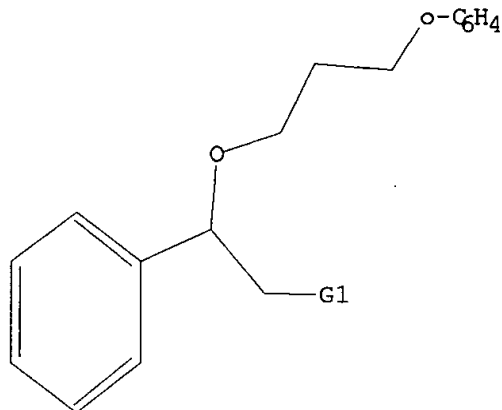
NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2 Apr 08 "Ask CAS" for self-help around the clock  
NEWS 3 Jun 03 New e-mail delivery for search results now available  
NEWS 4 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN  
NEWS 5 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)  
now available on STN  
NEWS 6 Aug 26 Sequence searching in REGISTRY enhanced  
NEWS 7 Sep 03 JAPIO has been reloaded and enhanced  
NEWS 8 Sep 16 Experimental properties added to the REGISTRY file  
NEWS 9 Sep 16 CA Section Thesaurus available in CAPLUS and CA  
NEWS 10 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985  
NEWS 11 Oct 24 BEILSTEIN adds new search fields  
NEWS 12 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN  
NEWS 13 Nov 18 DKILIT has been renamed APOLLIT  
NEWS 14 Nov 25 More calculated properties added to REGISTRY  
NEWS 15 Dec 04 CSA files on STN  
NEWS 16 Dec 17 PCTFULL now covers WP/PCT Applications from 1978 to date  
NEWS 17 Dec 17 TOXCENTER enhanced with additional content  
NEWS 18 Dec 17 Adis Clinical Trials Insight now available on STN  
NEWS 19 Jan 29 Simultaneous left and right truncation added to COMPENDEX,  
ENERGY, INSPEC  
NEWS 20 Feb 13 CANCERLIT is no longer being updated  
NEWS 21 Feb 24 METADEX enhancements  
NEWS 22 Feb 24 PCTGEN now available on STN  
NEWS 23 Feb 24 TEMA now available on STN  
NEWS 24 Feb 26 NTIS now allows simultaneous left and right truncation  
NEWS 25 Feb 26 PCTFULL now contains images  
NEWS 26 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results  
NEWS 27 Mar 20 EVENTLINE will be removed from STN  
NEWS 28 Mar 24 PATDPAFULL now available on STN  
NEWS 29 Mar 24 Additional information for trade-named substances without  
structures available in REGISTRY  
NEWS 30 Apr 11 Display formats in DGENE enhanced  
NEWS 31 Apr 14 MEDLINE Reload  
NEWS 32 Apr 17 Polymer searching in REGISTRY enhanced  
NEWS 33 Apr 21 Indexing from 1947 to 1956 being added to records in CA/CAPLUS  
NEWS 34 Apr 21 New current-awareness alert (SDI) frequency in  
WPIDS/WPINDEX/WPIX  
NEWS 35 Apr 28 RDISCLOSURE now available on STN  
NEWS 36 May 05 Pharmacokinetic information and systematic chemical names  
added to PHAR  
NEWS 37 May 15 MEDLINE file segment of TOXCENTER reloaded  
NEWS 38 May 15 Supporter information for ENCOMPPAT and ENCOMPLIT updated  
NEWS 39 May 16 CHEMREACT will be removed from STN

L1 STRUCTURE UPLOADED

=&gt; d l1

L1 HAS NO ANSWERS

L1 STR



G1 NH,X,Hy

Structure attributes must be viewed using STN Express query preparation.

=&gt; s l1

SAMPLE SEARCH INITIATED 14:29:55 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 3808 TO ITERATE

26.3% PROCESSED 1000 ITERATIONS

0 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 72461 TO 79859

PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=&gt; s l1 sss full

FULL SEARCH INITIATED 14:30:01 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 74649 TO ITERATE

100.0% PROCESSED 74649 ITERATIONS

55 ANSWERS

SEARCH TIME: 00.00.04

L3 55 SEA SSS FUL L1

=&gt; file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

148.15

148.36

FILE 'CAPLUS' ENTERED AT 14:30:10 ON 26 MAY 2003



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FILE COVERS 1907 - 26 May 2003 VOL 138 ISS 22  
FILE LAST UPDATED: 25 May 2003 (20030525/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13

L4 22 L3

=> d 14 fbib hitstr abs total

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 2001:568374 CAPLUS

DN 135:152793

TI Preparation of optically active oxazolidinedione derivatives for treatment of diabetes, hyperlipidemia, inflammation, and arteriosclerosis

IN Momose, Yu; Kodaka, Hiroyuki

PA Takeda Chemical Industries, Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 15 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

|    | PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---------------|------|----------|-----------------|----------|
|    | -----         | ---  | -----    | -----           | -----    |
| PI | JP 2001213880 | A2   | 20010807 | JP 2000-24773   | 20000128 |
|    |               |      |          | JP 2000-24773   | 20000128 |

IT 352662-19-2P

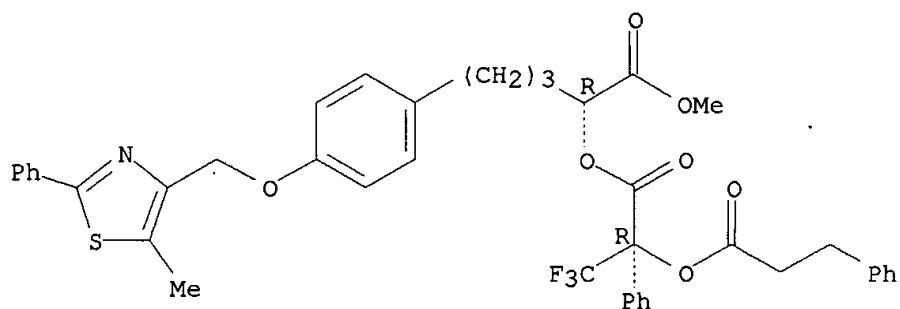
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of optically active oxazolidinedione derivs. for treatment of diabetes and hyperlipidemia and inflammation and arteriosclerosis)

RN 352662-19-2 CAPLUS

CN Benzenepentanoic acid, 4-[(5-methyl-2-phenyl-4-thiazolyl)methoxy]-.alpha.-[(2R)-3,3,3-trifluoro-1-oxo-2-(1-oxo-3-phenylpropoxy)-2-phenylpropoxy]-, monomethyl ester, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Claimed are (R)-(+)-5-[3-[4-[(5-methyl-2-phenyl-4-thiazolyl)methoxy]phenyl]propyl]-2,4-oxazolidinedione (I), salts and crystals thereof. Also claimed is the prepn. of I by cyclization of (R)-2-ethoxycarbonyloxy-5-[4-[(5-methyl-2-phenyl-4-thiazolyl)methoxy]phenyl]pentanamide. I at 0.2 mg/kg/day for one week gave 18% decrease of plasma glucose in Wistar fatty rats. Formulations are given.

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 2001:57805 CAPLUS

DN 134:252075

TI Synthesis of enantiopure homoallylic ethers by reagent controlled facial selective allylation of chiral ketones

AU Tietze, Lutz F.; Weigand, Berthold; Volkel, Ludwig; Wulff, Christian; Bittner, Christian

CS Institut für Organische Chemie Georg-August-Universität Göttingen, Göttingen, 37077, Germany

SO Chemistry--A European Journal (2001), 7(1), 161-168

CODEN: CEUJED; ISSN: 0947-6539

PB Wiley-VCH Verlag GmbH

DT Journal

LA English

OS CASREACT 134:252075

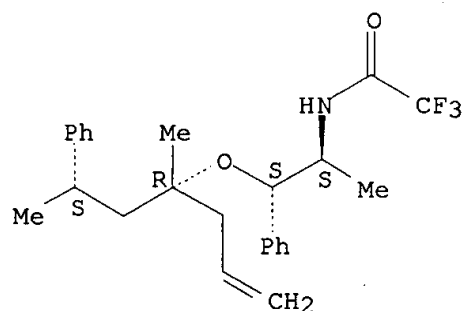
IT **330798-68-0P 330798-69-1P**

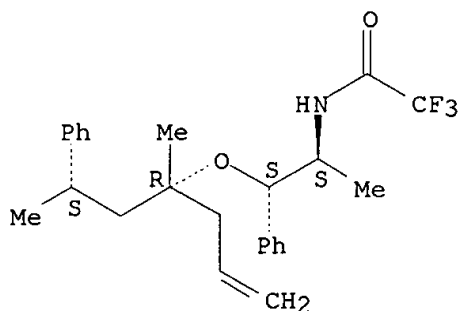
RL: BYP (Byproduct); SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of enantiopure homoallylic ethers by reagent controlled facial selective allylation of chiral ketones)

RN 330798-68-0 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1S,2S)-1-methyl-2-[[[(1R)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

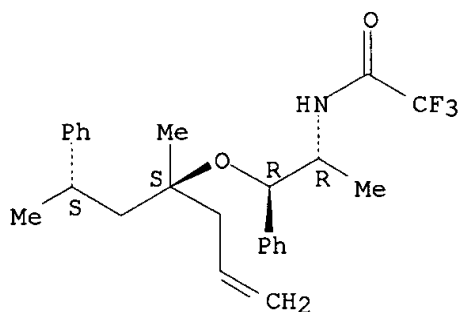




RN 330798-69-1 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[[(1S)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 330798-62-4P 330798-63-5P 330798-73-7P

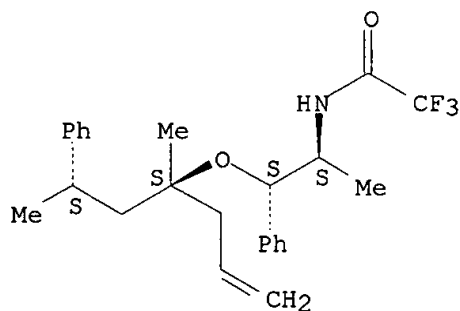
330798-76-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of enantiopure homoallylic ethers by reagent controlled  
facial selective allylation of chiral ketones)

RN 330798-62-4 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1S,2S)-1-methyl-2-[[[(1S)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

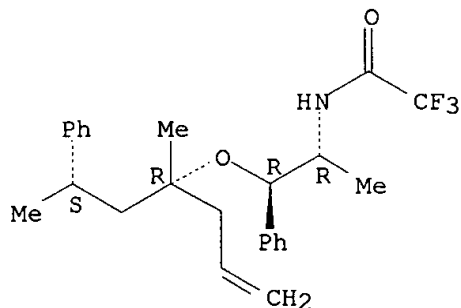
Absolute stereochemistry. Rotation (-).



RN 330798-63-5 CAPLUS

CN    Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1R)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]- (9CI)    (CA INDEX NAME)

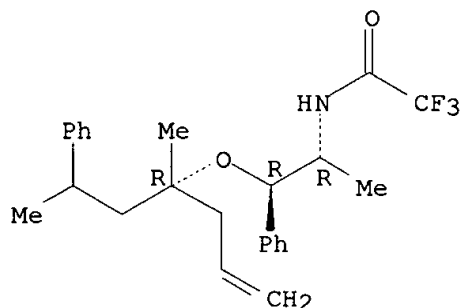
Absolute stereochemistry. Rotation (+).



RN 330798-73-7 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1R)-1-methyl-1-(2-phenylpropyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

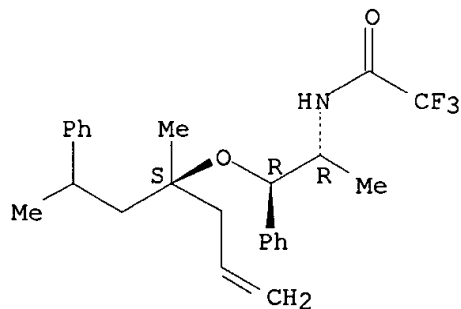
Absolute stereochemistry.



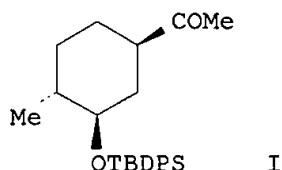
RN 330798-76-0 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1S)-1-methyl-1-(2-phenylpropyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI

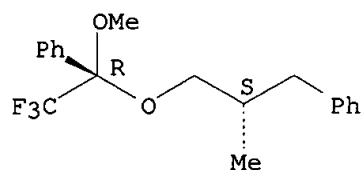


AB The stereoselective allylation of chiral Me ketones to give tertiary homoallylic ethers, which can easily be transformed into homoallylic alcs., is described. Reaction of the enantiopure ketones (I), (R)-Me<sub>2</sub>CH(CH<sub>2</sub>)<sub>3</sub>CH(.beta.Me)CH<sub>2</sub>COMe, (R)-MeCH(.beta.OSiPh<sub>2</sub>CMe<sub>3</sub>)CH<sub>2</sub>COMe, (S)-MeCH(.alpha.Ph)CH<sub>2</sub>COMe and the racemic ketones MeCH(OSiPh<sub>2</sub>CMe<sub>3</sub>)CH<sub>2</sub>COMe, MeCH(Ph)CH<sub>2</sub>COMe, MeCH<sub>2</sub>CH(Ph)COMe, MeCH<sub>2</sub>CH(Me)COMe with the norpseudoephedrine deriv. and allylsilane in the presence of a catalytic amt. of trifluoromethanesulfonic acid, led to a series of homoallylic ethers with good to excellent diastereoselectivity (85:15 to > 97:3). The allylation is reagent controlled and nearly independent from the stereogenic centers in the substrates. A partial kinetic resolu. was obsd. using the racemic ketones. In the reaction of the chiral ketones with the achiral reagents ethoxytrimethylsilane and allylsilane only a low diastereoselectivity was obsd.

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2003 ACS  
AN 2000:845053 CAPLUS  
DN 134:115714  
TI SuperQuat, (S)-4-benzyl-5,5-dimethyloxazolidin-2-one for the asymmetric synthesis of .alpha.-substituted aldehydes  
AU Bull, Steven D.; Davies, Stephen G.; Nicholson, Rebecca L.; Sanganee, Hitesh J.; Smith, Andrew D.  
CS The Dyson Perrins Laboratory, University of Oxford, Oxford, OX1 3QY, UK  
SO Tetrahedron: Asymmetry (2000), 11(17), 3475-3479  
CODEN: TASYE3; ISSN: 0957-4166  
PB Elsevier Science Ltd.  
DT Journal  
LA English  
OS CASREACT 134:115714  
IT 320606-37-9P 320606-39-1P 320606-41-5P  
320606-43-7P 320606-45-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(using (S)-4-benzyl-5,5-dimethyloxazolidin-2-one for the asym. synthesis of .alpha.-substituted aldehydes)  
RN 320606-37-9 CAPLUS  
CN Benzene, [(2S)-2-methyl-3-[(1R)-2,2,2-trifluoro-1-methoxy-1-phenylethoxy]propyl]- (9CI) (CA INDEX NAME)

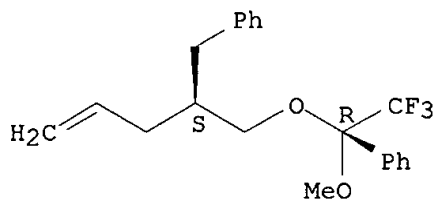
Absolute stereochemistry.



RN 320606-39-1 CAPLUS

CN Benzene, [(2S)-2-[[[(1R)-2,2,2-trifluoro-1-methoxy-1-phenylethoxy]methyl]-4-pentenyl]- (9CI) (CA INDEX NAME)

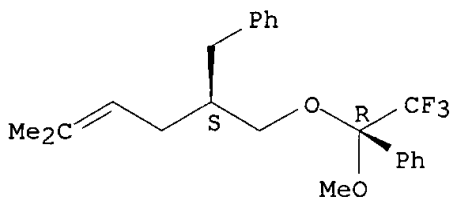
Absolute stereochemistry.



RN 320606-41-5 CAPLUS

CN Benzene, [(2S)-5-methyl-2-[[[(1R)-2,2,2-trifluoro-1-methoxy-1-phenylethoxy]methyl]-4-hexenyl]- (9CI) (CA INDEX NAME)

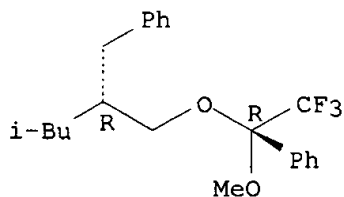
Absolute stereochemistry.



RN 320606-43-7 CAPLUS

CN Benzene, [(2R)-4-methyl-2-[[[(1R)-2,2,2-trifluoro-1-methoxy-1-phenylethoxy]methyl]pentyl]- (9CI) (CA INDEX NAME)

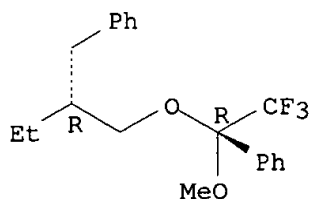
Absolute stereochemistry.



RN 320606-45-9 CAPLUS

CN Benzene, [(2R)-2-[[[(1R)-2,2,2-trifluoro-1-methoxy-1-phenylethoxy]methyl]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Redn. of .alpha.-substituted-(S)-N-acyl-4-benzyl-5,5-dimethyloxazolidin-2-ones with DIBAL-H in CH<sub>2</sub>Cl<sub>2</sub> affords .alpha.-substituted aldehydes with no loss of stereochem. integrity at their .alpha.-center.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 1999:292590 CAPLUS

DN 130:338021

TI Preparation of arylacetic amide derivatives as a preventive or remedy for urinary disorders

IN Kaihoh, Terumitsu; Okada, Tomomi; Takahashi, Yoshinori; Mizuno, Hiroyuki; Honda, Haruyoshi; Sato, Susumo

PA SSP Co., Ltd., Japan

SO Eur. Pat. Appl., 21 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.  | DATE     |
|----|---|------|----------|------------------|----------|
| PI | EP 913393   | A2   | 19990506 | EP 1998-120422   | 19981028 |
|    | EP 913393   | A3   | 19990526 |                  |          |
|    | EP 913393   | B1   | 20030212 |                  |          |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO |      |          |                  |          |
|    | JP 11193271   | A2   | 19990721 | JP 1997-300352 A | 19971031 |
|    |   |      |          | JP 1998-290576   | 19981013 |
|    |   |      |          | JP 1997-300352 A | 19971031 |
|    | US 6060485  | A    | 20000509 | US 1998-181091   | 19981028 |
|    |   |      |          | JP 1997-300352 A | 19971031 |
|    | CN 1222510  | A    | 19990714 | CN 1998-122655   | 19981030 |
|    |   |      |          | JP 1997-300352 A | 19971031 |
|    | TW 442470   | B    | 20010623 | TW 1998-87118071 | 19981030 |
|    |   |      |          | JP 1997-300352 A | 19971031 |

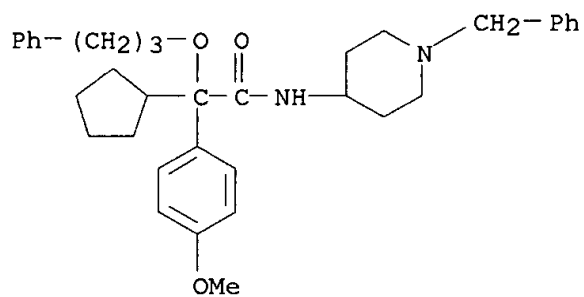
OS MARPAT 130:338021

IT 224034-69-9P 224034-79-1P 224034-80-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of arylacetic amide derivs. as a preventive or remedy for urinary disorders)

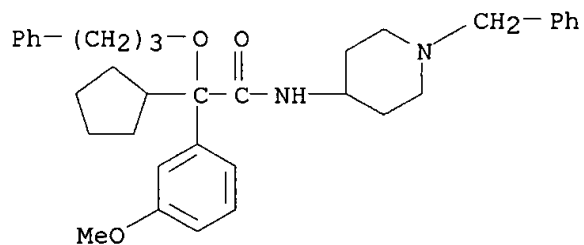
RN 224034-69-9 CAPLUS

CN Benzeneacetamide, .alpha.-cyclopentyl-4-methoxy-N-[1-(phenylmethyl)-4-piperidiny]-.alpha.-(3-phenylpropoxy)- (9CI) (CA INDEX NAME)



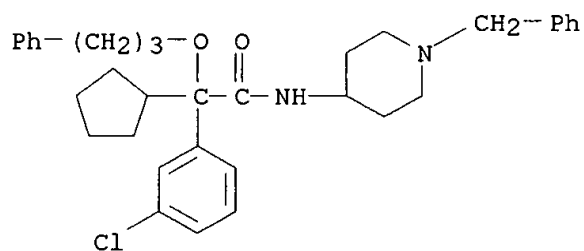
RN 224034-79-1 CAPLUS

CN Benzeneacetamide, .alpha.-cyclopentyl-3-methoxy-N-[1-(phenylmethyl)-4-piperidinyl]-.alpha.-(3-phenylpropoxy)- (9CI) (CA INDEX NAME)

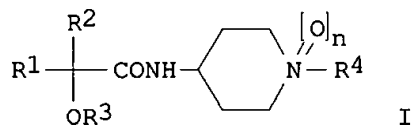


RN 224034-80-4 CAPLUS

CN Benzeneacetamide, 3-chloro-.alpha.-cyclopentyl-N-[1-(phenylmethyl)-4-piperidinyl]-.alpha.-(3-phenylpropoxy)- (9CI) (CA INDEX NAME)



GI



AB The title compds. [I; R1 = (un)substituted arom. hydrocarbon or heteroarom. group; R2, R3 = (un)substituted hydrocarbon or heterocyclic



group; R4 = H, (un)substituted hydrocarbon or heterocyclic group; n = 0-1] and their salts which have both excellent anticholinergic action and calcium antagonism and at the same time have high selectivity to bladder, so that they are useful as preventives or remedies for urinary disorders, were prepd. Thus, treatment of N-(1-benzyl-4-piperidiny1)-2-hydroxy-3-methyl-2-phenylbutanamide with NaH in DMF followed by addn. of BuI and a soln. of Bu4NI in DMF afforded 28% I [R1 = Ph; R2 = iPr; R3 = Bu; R4 = PhCH2; n = 0] which showed ID50 of 9.8 mg/kg against bladder contraction in rats.

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 1998:625620 CAPLUS

DN 129:316000

TI Synthesis of enantiopure homoallylic alcohols by a highly selective asymmetric allylation of ketones

AU Tietze, Lutz F.; Schiemann, Kai; Wegner, Christoph; Wulff, Christian

CS Institute Organic Chemistry, Georg-August-Universitat Gottingen, Gottingen, D-37077, Germany

SO Chemistry--A European Journal (1998), 4(9), 1862-1869

CODEN: CEUJED; ISSN: 0947-6539

PB Wiley-VCH Verlag GmbH

DT Journal

LA English

OS CASREACT 129:316000

IT 165823-95-0P

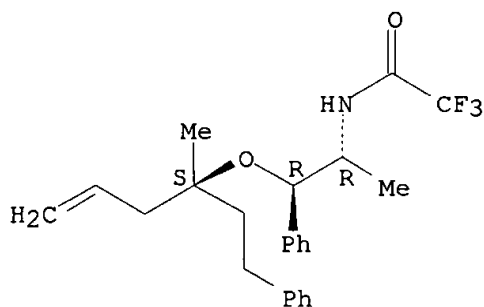
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of enantiopure homoallylic alcs. by asym. allylation of ketones)

RN 165823-95-0 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1S)-1-methyl-1-(2-phenylethyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



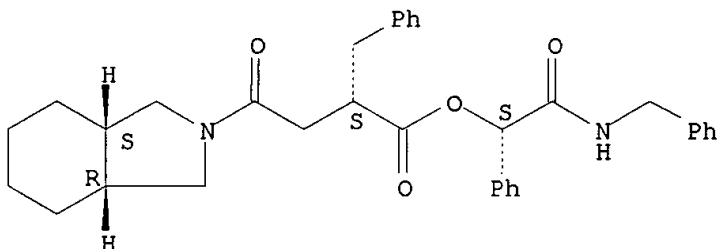
AB A highly selective asym. domino allylation of aliph. ketones is described. When Me ketones, (R,R)-Me2SiOCHPhCHMeNHCOCF3, and CH2:CHCH2SiMe3 react in the presence of catalytic amts. of trifluoromethanesulfonic acid, the homoallylic ethers are produced with up to 24:1 diastereoselectivity and 89% yield. Ether cleavage using lithium or sodium in liq. ammonia gives the homoallylic alcs. in 75 to 95% yield and up to 92% ee. Even EtCOMe, the most difficult example, showed a stereoselectivity of 9:1 at -78.degree.C and 24:1 at -109.degree.C. In addn., the allylation of protected hydroxyalkyl Me ketones gave the corresponding homoallylic

ethers with a diastereoselectivity of up to >244:1 and 98% yield. In contrast, Et alkyl ketones have a low selectivity.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

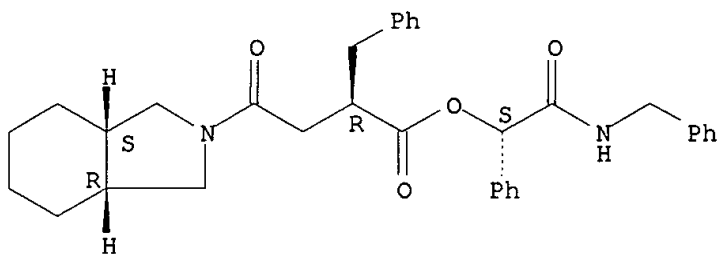
L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2003 ACS  
AN 1997:639948 CAPLUS  
DN 127:307269  
TI Preparation of optically active succinic acid derivatives. I. Optical resolution of 2-benzyl-3-(cis-hexahydroisoindolin-2-ylcarbonyl)propionic acid  
AU Yamaguchi, Toshiaki; Yanagi, Takashi; Hokari, Hiroshi; Mukaiyama, Yuko; Kamijo, Tetsuhide; Yamamoto, Iwao  
CS Kissei Pharmaceutical Co., Ltd., Central Research Laboratories, Hotaka, 399-83, Japan  
SO Chemical & Pharmaceutical Bulletin (1997), 45(9), 1518-1520  
CODEN: CPBTAL; ISSN: 0009-2363  
PB Pharmaceutical Society of Japan  
DT Journal  
LA English  
IT **197447-44-2P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(optical resolu. of benzyl(hexahydroisoindolinylcarbonyl)propionic acid)  
RN 197447-44-2 CAPLUS  
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, 2-oxo-1-phenyl-2-[(phenylmethyl)amino]ethyl ester, [2(.alpha.S)-[2[R\*(R\*)],3a.alpha.,7a.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **197447-45-3P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(optical resolu. of benzyl(hexahydroisoindolinylcarbonyl)propionic acid)  
RN 197447-45-3 CAPLUS  
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, 2-oxo-1-phenyl-2-[(phenylmethyl)amino]ethyl ester, [2(.alpha.R)-[2[R\*(S\*)],3a.alpha.,7a.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB Optical resolu. of 2-benzyl-3-(cis-hexahydroisoidolin-2-ylcarbonyl)propionic acid (I) was accomplished by two methods. Thus, I was esterified with (S)-N-benzylmandelamide and the resulting diastereomeric esters were sepd. by column chromatog. on silica gel. One of the diastereomers was hydrolyzed to give the optically active acid (-)-I. The abs. configuration of (-)-I was established as S by comparison with an authentic sample. The alternative method was resolu. using an optically active amine. Treatment of a soln. of the racemic acid I with 0.65 equiv of (R)-1-(1-naphthyl)ethylamine in ethanol gave the salt in 23.2% yield with an optical purity of 96.8% ee.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 1996:96240 CAPLUS

DN 124:260514

TI Transformations of isoxazolidine and dihydropyran derivatives to optically active compounds

AU Diaz-Ortiz, Angel; Diez-Barra, Enrique; de la Hoz, Antonio; Prieto, Pilar; Moreno, Andres

CS Fac. Quimica, Univ. Castilla-La Mancha, Ciudad Real, E-13071, Spain

SO Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1996), (3), 259-63

CODEN: JCPRB4; ISSN: 0300-922X

PB Royal Society of Chemistry

DT Journal

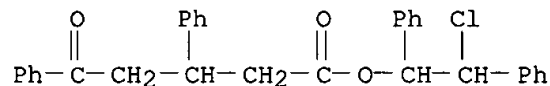
LA English

IT **174814-84-7P**

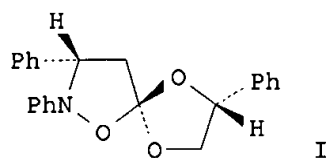
RL: SPN (Synthetic preparation); PREP (Preparation)  
(hydrolysis and hydrogenation of spiroisoxazolidines and spirodihydropyrans)

RN 174814-84-7 CAPLUS

CN Benzenepentanoic acid, .delta.-oxo-.beta.-phenyl-, 2-chloro-1,2-diphenylethyl ester (9CI) (CA INDEX NAME)



GI



AB Isoxazolidine and dihydropyran spiro derivs., e.g. I, can be easily transformed, by hydrolysis and hydrogenolysis, to give .delta.-keto esters, .delta.-keto acids, .beta.-amino esters, e.g., (S)-MeO<sub>2</sub>CCH<sub>2</sub>CHPhNPhCl, .beta.-amino acids and 3-amino alcs. in good yields. Starting from optically active compds., enantiomerically pure products are obtained. In some cases, reactions were induced by microwave irradiation.

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 1995:835557 CAPLUS

DN 123:256542

TI Preparation of annelated dihydropyridines

IN Roos, Otto; Loesel, Walter; Arndts, Dietrich

PA Boehringer Ingelheim KG, Germany

SO Ger. Offen., 28 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.  | DATE     |
|----|---|------|----------|------------------|----------|
| PI | DE 4343683  | A1   | 19950622 | DE 1993-4343683  | 19931221 |
|    | CA 2178209  | AA   | 19950629 | CA 1994-2178209  | 19941214 |
|    |   |      |          | DE 1993-4343683A | 19931221 |
|    | WO 9517389  | A1   | 19950629 | WO 1994-EP4150   | 19941214 |
|    | W: AU, CA, CN, JP, KR, PL, RU   |      |          |                  |          |
|    | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE    |      |          |                  |          |
|    |   |      |          | DE 1993-4343683A | 19931221 |
|    | AU 9512433  | A1   | 19950710 | AU 1995-12433    | 19941214 |
|    | AU 699208   | B2   | 19981126 |                  |          |
|    |   |      |          | DE 1993-4343683A | 19931221 |
|    |   |      |          | WO 1994-EP4150 W | 19941214 |
|    | EP 736011   | A1   | 19961009 | EP 1995-903342   | 19941214 |
|    | EP 736011   | B1   | 20000726 |                  |          |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE |      |          |                  |          |
|    |   |      |          | DE 1993-4343683A | 19931221 |
|    |   |      |          | WO 1994-EP4150 W | 19941214 |
|    | CN 1138325  | A    | 19961218 | CN 1994-194572   | 19941214 |
|    | CN 1044905  | B    | 19990901 |                  |          |
|    |   |      |          | DE 1993-4343683A | 19931221 |
|    | JP 09506882   | T2   | 19970708 | JP 1994-517154   | 19941214 |
|    |   |      |          | DE 1993-4343683A | 19931221 |
|    |   |      |          | WO 1994-EP4150 W | 19941214 |
|    | RU 2136664  | C1   | 19990910 | RU 1996-115153   | 19941214 |
|    |   |      |          | DE 1993-4343683A | 19931221 |
|    |   |      |          | WO 1994-EP4150 W | 19941214 |
|    | AT 194978   | E    | 20000815 | AT 1995-903342   | 19941214 |
|    |   |      |          | DE 1993-4343683A | 19931221 |

|            |    |          |                           |
|------------|----|----------|---------------------------|
| ES 2149958 | T3 | 20001116 | WO 1994-EP4150 W 19941214 |
| ZA 9410115 | A  | 19950621 | ES 1995-903342 19941214   |
| US 5661157 | A  | 19970826 | DE 1993-4343683A 19931221 |
| TW 404941  | B  | 20000911 | ZA 1994-10115 19941220    |
| US 5968948 | A  | 19991019 | DE 1993-4343683A 19931221 |
| US 6136819 | A  | 20001024 | US 1994-360867 19941221   |
|            |    |          | DE 1993-4343683A 19931221 |
|            |    |          | TW 1994-83112295 19941228 |
|            |    |          | DE 1993-4343683A 19931221 |
|            |    |          | US 1997-857643 19970516   |
|            |    |          | DE 1993-4343683A 19931221 |
|            |    |          | US 1994-360867 A319941221 |
|            |    |          | US 1999-329443 19990610   |
|            |    |          | DE 1993-4343683A 19931221 |
|            |    |          | US 1994-360867 A319941221 |
|            |    |          | US 1997-857643 A319970516 |

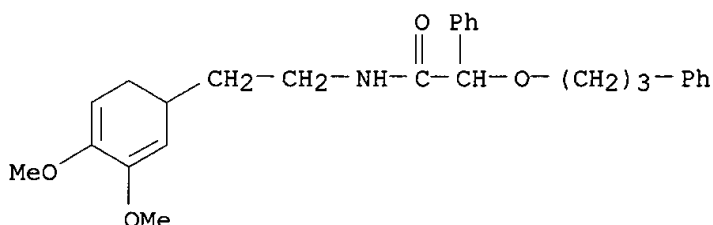
OS MARPAT 123:256542

IT **168545-16-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of annelated dihydropyridines from)

RN 168545-16-2 CAPLUS

CN Benzeneacetamide, N-[2-(3,4-dimethoxy-2,4-cyclohexadien-1-yl)ethyl]-  
.alpha.-(3-phenylpropoxy)- (9CI) (CA INDEX NAME)



GI For diagram(s), see printed CA Issue.

AB The title compds. [I; A = benzo, thieno, indolo; B = O, S, (un)substituted CH2; R2 = OH, alkoxy, benzyloxy, halogen, alkyl, methanesulfonyloxy, etc.; R3 = 2- or 3-thienyl, (un)substituted Ph, alkyl, cycloalkylalkyl; R4 = (un)branched alkenyl or alkynyl, alkoxy, dialkylamino, heterocyclyl, Ph, etc.; m = 0-3] (e.g., II), useful as calcium-channel blockers (no data), are prepd. by the intramol. cyclocondensation of arom. amides (III) (e.g., IV) in the presence of condensing agents (e.g., POCl3), and I-contg. formulations are also presented.

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 1995:568922 CAPLUS

DN 123:111518

TI Enantioselective Synthesis of Tertiary Homoallylic Alcohols via  
Diastereoselective Addition of Allylsilanes to Ketones

AU Tietze, Lutz F.; Schiemann, Kai; Wegner, Christoph

CS Institute of Organic Chemistry, Georg-August-Universitaet, Goettingen,  
D-37077, Germany

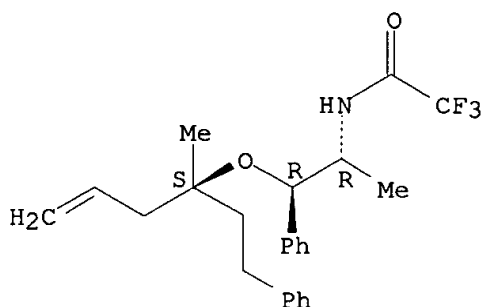
SO Journal of the American Chemical Society (1995), 117(21), 5851-2

CODEN: JACSAT; ISSN: 0002-7863

PB American Chemical Society

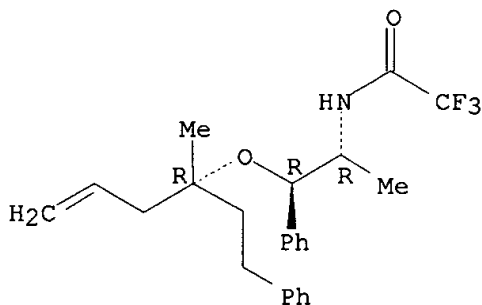
DT Journal  
 LA English  
 OS CASREACT 123:111518  
 IT **165823-95-0P 166021-67-6P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (enantioselective synthesis of tertiary homoallylic alcs. via  
 diastereoselective addn. of allylsilanes to ketones)  
 RN 165823-95-0 CAPLUS  
 CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1S)-1-methyl-1-(2-phenylethyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



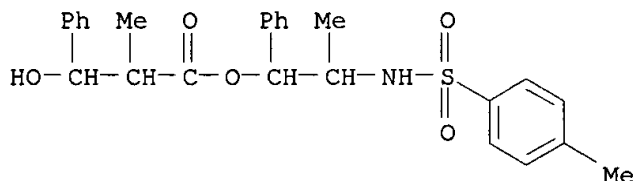
RN 166021-67-6 CAPLUS  
 CN Acetamide, 2,2,2-trifluoro-N-[1-methyl-2-[[1-methyl-1-(2-phenylethyl)-3-butenyl]oxy]-2-phenylethyl]-, [1R-[1R\*,2R\*(R\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

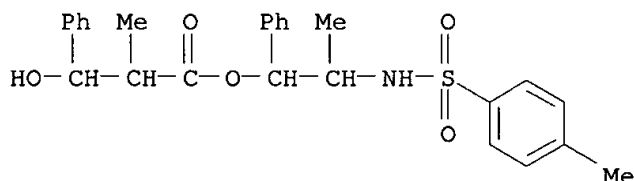


AB Enantiopure tertiary homoallylic alcs.  $\text{CH}_2\text{:CHCH}_2\text{CRMeOH}$  ( $\text{R} = \text{alkyl}$ ) can be obtained from the corresponding homoallylic ethers  $\text{CH}_2\text{:CHCH}_2\text{CRMeOR}_1$  [4,  $\text{R}_1 = \text{residue of (1R,2R)-N-(trifluoroacetyl)norpseudoephedrine}$ ] by treatment with sodium in liq. ammonia. The ethers 4 are formed highly selectively by treatment of the ketones  $\text{MeCOR}$  with the trimethylsilyl ether of N-trifluoroacetylnorpseudoephedrine in the presence of catalytic amts. of  $\text{Me}_3\text{SiB(OTf)}_4$  or  $\text{Me}_3\text{SiOTf/TfOH}$  ( $\text{Tf} = \text{CF}_3\text{SO}_2$ ) followed by addn. of allyltrimethylsilane. The yield was about 90% (based on conversion) and the diastereoselectivity was about 90:10. Using iso-Pr Me ketone a selectivity of >95:5 was obtained; thus only one diastereomer could be detected.

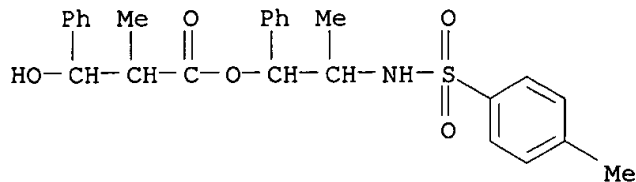
L4 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2003 ACS  
AN 1992:213702 CAPLUS  
DN 116:213702  
TI Stereoselective aldol reactions. Reaction of chiral ester titanium enolate with aldehydes  
AU Xiang, Yibin; Olivier, Eric; Ouimet, Nathalie  
CS Merck Frosst Cent. Ther. Res., Pointe Claire-Dorval, QC, H9R 4P8, Can.  
SO Tetrahedron Letters (1992), 33(4), 457-60  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
OS CASREACT 116:213702  
IT **139954-97-5P 140147-55-3P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)  
RN 139954-97-5 CAPLUS  
CN Benzenepropanoic acid, .beta.-hydroxy-.alpha.-methyl-,  
2-[[[(4-methylphenyl)sulfonyl]amino]-1-phenylpropyl ester,  
[.alpha.S-[.alpha.R\*(1S\*,2R\*),.beta.S\*]]- (9CI) (CA INDEX NAME)



RN 140147-55-3 CAPLUS  
CN Benzenepropanoic acid, .beta.-hydroxy-.alpha.-methyl-,  
2-[[[(4-methylphenyl)sulfonyl]amino]-1-phenylpropyl ester,  
[.alpha.R-[.alpha.R\*(1R\*,2S\*),.beta.R\*]]- (9CI) (CA INDEX NAME)

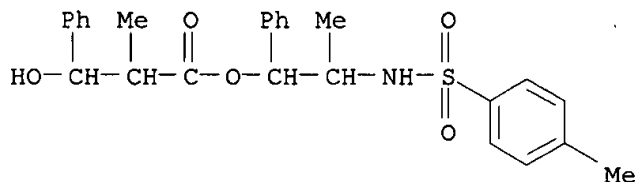


IT **140147-56-4P 141117-22-8P**  
RL: PREP (Preparation)  
(stereoselective synthesis of)  
RN 140147-56-4 CAPLUS  
CN Benzenepropanoic acid, .beta.-hydroxy-.alpha.-methyl-,  
2-[[[(4-methylphenyl)sulfonyl]amino]-1-phenylpropyl ester,  
[.alpha.S-[.alpha.R\*(1S\*,2R\*),.beta.R\*]]- (9CI) (CA INDEX NAME)

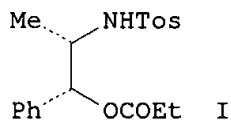


RN 141117-22-8 CAPLUS

CN Benzenepropanoic acid, .beta.-hydroxy-.alpha.-methyl-,  
 2-[[ (4-methylphenyl) sulfonyl] amino]-1-phenylpropyl ester,  
 [.alpha.R- [.alpha.R\*(1R\*,2S\*), .beta.S\*]]- (9CI) (CA INDEX NAME)



GI



AB The chiral ester I was enolized under  $\text{TiCl}_4/\text{Et}_3\text{N}$  conditions and reacted with aldehydes to give moderate to good stereoselectivities. Thus, successive treatment of I with  $\text{TiCl}_4$  in  $\text{CH}_2\text{Cl}_2$ ,  $\text{Et}_3\text{N}$ , and preformed  $\text{BzH-TiCl}_4$  complex gave 85% syn aldol. The chiral auxiliary group can be removed by simple sapon. and recovered.

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 1989:553339 CAPLUS

DN 111:153339

TI Preparation of esterified N-(dibenzocycloheptenylideneethyl)ephedrine derivatives with prolonged antiulcer activity

IN Butelman, Federico

PA Etablissement Texcontor, Liechtenstein

SO Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 313885   | A1   | 19890503 | EP 1988-116449  | 19881005 |
|    | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                 |          |
|    | US 4935444  | A    | 19900619 | IT 1987-22407   | 19871023 |
|    |   |      |          | US 1988-254220  | 19881006 |
|    |   |      |          | IT 1987-22407   | 19871023 |



|             |    |          |                |          |
|-------------|----|----------|----------------|----------|
| JP 01135748 | A2 | 19890529 | JP 1988-264240 | 19881021 |
|             |    |          | IT 1987-22407  | 19871023 |
| US 4990522  | A  | 19910205 | US 1990-487277 | 19900302 |
|             |    |          | IT 1987-22407  | 19871023 |
|             |    |          | US 1988-254220 | 19881006 |

IT **122881-51-0P**

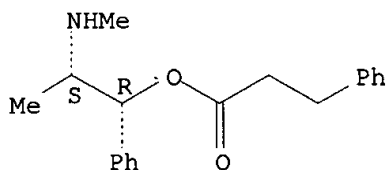
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and N-alkylation of, with (haloethylidene)dibenzocycloheptene)

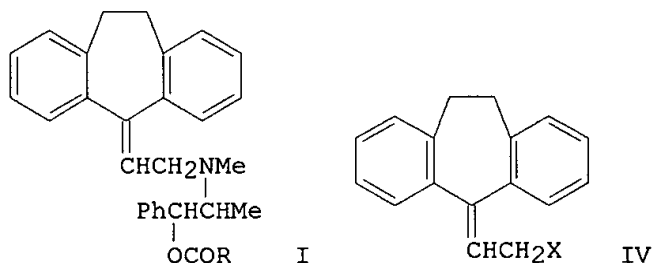
RN 122881-51-0 CAPLUS

CN Benzenepropanoic acid, 2-(methylamino)-1-phenylpropyl ester, [R-(R\*,S\*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB Title compds. [I; R = C<sub>9</sub>H<sub>19</sub>, C<sub>15</sub>H<sub>31</sub>, CH(NH<sub>2</sub>)(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H, (CH<sub>2</sub>)<sub>2</sub>Ph, CMe<sub>3</sub>, p-HOC<sub>6</sub>H<sub>4</sub>, 2-thienyl, 3-pyridyl, 1-amino-2-(5-imidazolyl)ethyl, pamoic acid residue] are prepd. by esterification of ephedrine (II) with RCOCl to give PhCH(O<sub>2</sub>CR)CHMeNHMe (III), followed by N-alkylation with a (haloethylidene)dibenzocycloheptene IV (X = halo). II was esterified by decanoyl chloride (prepd. from the acid) to give 65% III [R = Me(CH<sub>2</sub>)<sub>8</sub>], which was refluxed in MeCN with IV (X = halo, not specified) to give 54% I [R = MeC(CH<sub>2</sub>)<sub>2</sub>]. The latter inhibited stress-induced ulcers in rats with ED<sub>50</sub> of 0.4 and 2.1 mg/kg orally, administered 6 and 36 h prior to commencement of the stress, resp.

L4 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 1988:150014 CAPLUS

DN 108:150014

TI Stereoselective aldol reactions with (R)- and (S)-2-hydroxy-1,2,2-triphenylethyl acetate and related glycol monoacetates

AU Devant, Ralf; Mahler, Ulrike; Braun, Manfred

CS Inst. Org. Chem. Makromol. Chem., Univ. Duesseldorf, Duesseldorf, D-4000/1, Fed. Rep. Ger.

SO Chemische Berichte (1988), 121(3), 397-406

CODEN: CHBEAM; ISSN: 0009-2940

DT Journal

LA German

OS CASREACT 108:150014

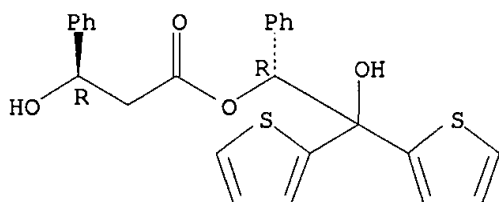
IT **110744-05-3P 110744-06-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and base hydrolysis of)

RN 110744-05-3 CAPLUS

CN Benzenepropanoic acid, .beta.-hydroxy-, 2-hydroxy-1-phenyl-2,2-di-2-thienylethyl ester, [R-(R\*,R\*)]- (9CI) (CA INDEX NAME)

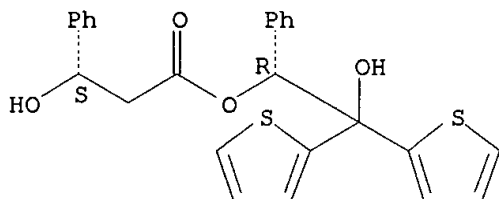
Absolute stereochemistry.



RN 110744-06-4 CAPLUS

CN Benzenepropanoic acid, .beta.-hydroxy-, 2-hydroxy-1-phenyl-2,2-di-2-thienylethyl ester, [R-(R\*,S\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The enolate  $\text{H}_2\text{C}:\text{C}(\text{OM})\text{OCHPhCPh}_2\text{OM}$  (I;  $\text{M} = \text{Li}, \text{K}, \text{MgCl}$  etc.), formed by double deprotonation of the ester  $\text{HOCPh}_2\text{CHPhO}_2\text{CMe}$  (II), is added to aldehydes. The influences of the enolate gegenion, of the solvent, and of the reaction temp. on the ratio of the isomeric products  $\text{RC}(\text{OH})\text{CO}_2\text{CHPhCPh}_2\text{OH}$  (III;  $\text{R} = \text{Ph}, \text{CHMe}_2, (\text{CH}_2)_3\text{Me}$ ) are studied. The highest degrees of diastereoselectivity were obtained when the magnesium enolate I ( $\text{M} = \text{MgX}$ ) was used. The basic hydrolysis of the adducts III affords .beta.-hydroxy carboxylic acids in corresponding optical purity. Thereby, the chiral auxiliary reagent,  $\text{HOCHPhCPh}_2\text{OH}$  (IV), is recovered. The aldol reaction of the doubly deprotonated esters  $\text{MeCO}_2\text{CHPhR}$  [ $\text{R} = \text{bis}(\text{naphthyl})\text{hydroxymethyl}, \text{bis}(2\text{-methoxyphenyl})\text{hydroxymethyl}, \text{bis}(2\text{-thienyl})\text{hydroxymethyl}$ ] points to the structural parameters, which might be responsible for the high diastereoselectivity of the acetate II. In the mass spectra of IV, II,  $\text{MeCO}_2\text{CHPhCR}_1\text{OH}$  ( $\text{R}_1 = 4\text{-MeOC}_6\text{H}_4, 2\text{-thienyl}$ ), and their deprotonated products, unusual rearrangements were obsd.

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 1984:591513 CAPLUS  
 DN 101:191513  
 TI Cephalosporin derivatives, and prophylactic and therapeutic agents for bacterial infection  
 IN Kakeya, Nobuharu; Nishizawa, Susumu; Tamaki, Satoshi; Kitao, Kazuhiko  
 PA Kyoto Pharmaceutical Industries, Ltd., Japan  
 SO Eur. Pat. Appl., 84 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 2

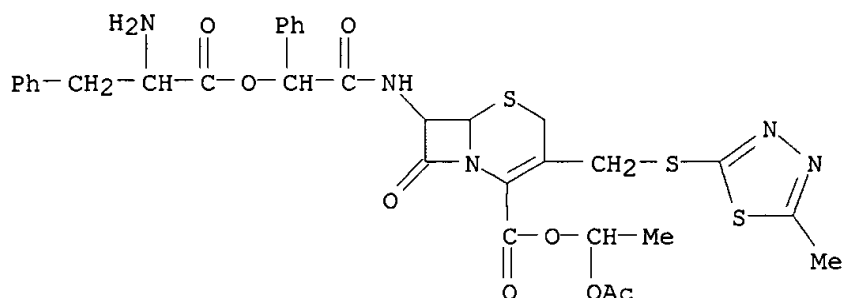
|    | PATENT NO.                                | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 108942                                 | A2   | 19840523 | EP 1983-110284  | 19831015 |
|    | EP 108942                                 | A3   | 19850515 |                 |          |
|    | EP 108942                                 | B1   | 19880302 |                 |          |
|    | R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE |      |          |                 |          |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | WO 8401949                                | A1   | 19840524 | WO 1982-JP437   | 19821110 |
|    | W: MC                                     |      |          |                 |          |
|    | US 4605651                                | A    | 19860812 | US 1983-540676  | 19831011 |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | ZA 8307635                                | A    | 19841128 | ZA 1983-7635    | 19831013 |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | AU 8320199                                | A1   | 19840517 | AU 1983-20199   | 19831014 |
|    | AU 568094                                 | B2   | 19871217 |                 |          |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | AT 32724                                  | E    | 19880315 | AT 1983-110284  | 19831015 |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    |   |      |          | EP 1983-110284  | 19831015 |
|    | NO 8303807                                | A    | 19840511 | NO 1983-3807    | 19831019 |
|    | NO 162240                                 | B    | 19890821 |                 |          |
|    | NO 162240                                 | C    | 19891129 |                 |          |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | ES 526561                                 | A1   | 19850416 | ES 1983-526561  | 19831019 |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | SU 1331432                                | A3   | 19870815 | SU 1983-3655401 | 19831019 |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | FI 8303839                                | A    | 19840511 | FI 1983-3839    | 19831020 |
|    | FI 75348                                  | B    | 19880229 |                 |          |
|    | FI 75348                                  | C    | 19880609 |                 |          |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | DK 8304818                                | A    | 19840511 | DK 1983-4818    | 19831020 |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | JP 59116292                               | A2   | 19840705 | JP 1983-197458  | 19831020 |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | CA 1239928                                | A1   | 19880802 | CA 1983-439358  | 19831020 |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | ES 532996                                 | A1   | 19850816 | ES 1984-532996  | 19840531 |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | ES 532997                                 | A1   | 19850816 | ES 1984-532997  | 19840531 |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | SU 1322983                                | A3   | 19870707 | SU 1984-3827995 | 19841224 |
|    |   |      |          | WO 1982-JP437   | 19821110 |

## PATENT FAMILY INFORMATION:

FAN 1987:636362

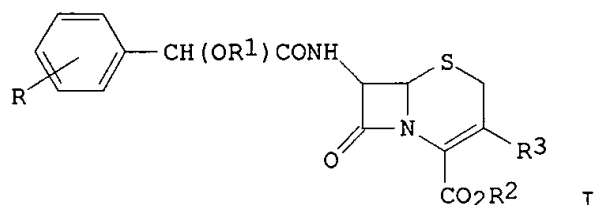
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

|    |  |    |          |                 |          |
|----|--|----|----------|-----------------|----------|
| PI | SU 1309912   | A3 | 19870507 | SU 1984-3826171 | 19841224 |
|    | WO 8401949   | A1 | 19840524 | WO 1982-JP437   | 19821110 |
|    | W: MC  |    |          | WO 1982-JP437   | 19821110 |
|    | US 4605651   | A  | 19860812 | US 1983-540676  | 19831011 |
|    | ZA 8307635   | A  | 19841128 | WO 1982-JP437   | 19821110 |
|    | AU 8320199   | A1 | 19840517 | ZA 1983-7635    | 19831013 |
|    | AU 568094  | B2 | 19871217 | WO 1982-JP437   | 19821110 |
|    | NO 8303807   | A  | 19840511 | AU 1983-20199   | 19831014 |
|    | NO 162240  | B  | 19890821 | WO 1982-JP437   | 19821110 |
|    | NO 162240  | C  | 19891129 | NO 1983-3807    | 19831019 |
|    | ES 526561  | A1 | 19850416 | WO 1982-JP437   | 19821110 |
|    | SU 1331432   | A3 | 19870815 | ES 1983-526561  | 19831019 |
|    | FI 8303839   | A  | 19840511 | WO 1982-JP437   | 19821110 |
|    | FI 75348   | B  | 19880229 | SU 1983-3655401 | 19831019 |
|    | FI 75348   | C  | 19880609 | WO 1982-JP437   | 19821110 |
|    | DK 8304818   | A  | 19840511 | FI 1983-3839    | 19831020 |
|    | JP 59116292  | A2 | 19840705 | WO 1982-JP437   | 19821110 |
|    | CA 1239928   | A1 | 19880802 | DK 1983-4818    | 19831020 |
|    | ES 532996  | A1 | 19850816 | WO 1982-JP437   | 19821110 |
|    | ES 532997  | A1 | 19850816 | JP 1983-197458  | 19831020 |
|    | SU 1322983   | A3 | 19870707 | WO 1982-JP437   | 19821110 |
|    |  |    |          | CA 1983-439358  | 19831020 |
|    |  |    |          | WO 1982-JP437   | 19821110 |
|    |  |    |          | ES 1984-532996  | 19840531 |
|    |  |    |          | WO 1982-JP437   | 19821110 |
|    |  |    |          | ES 1984-532997  | 19840531 |
|    |  |    |          | WO 1982-JP437   | 19821110 |
|    |  |    |          | SU 1984-3827995 | 19841224 |
|    |  |    |          | WO 1982-JP437   | 19821110 |
| IT | <b>92602-27-2P</b>   |    |          |                 |          |
|    | RL: SPN (Synthetic preparation); PREP (Preparation)  |    |          |                 |          |
|    | (prepn. of)  |    |          |                 |          |
| RN | 92602-27-2 CAPLUS  |    |          |                 |          |
| CN | L-Phenylalanine, 2-[[2-[[1-(acetyloxy)ethoxy]carbonyl]-3-[[5-methyl-1,3,4-thiadiazol-2-yl]thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl]amino]-2-oxo-1-phenylethyl ester, monohydrochloride, [6R-[6.alpha.,7.beta.(R*)]]- (9CI) (CA INDEX NAME) |    |          |                 |          |



● HCl

GI



AB Cephalosporins I (R = H, OH; R<sub>1</sub> = amino acid residue; R<sub>2</sub> = 1-alkanoyloxyalkyl, 1-alkoxycarbonyloxyalkyl, phthalidyl, 5-methyl-2-oxo-1,3-dioxolan-4-ylmethyl; R<sub>3</sub> = carbamoyloxymethyl, heterocyclylthiomethyl) were prepd. Thus D-HOCHPhCO<sub>2</sub>CHPh<sub>2</sub> was treated with Me<sub>3</sub>CO<sub>2</sub>CNHCH<sub>2</sub>CO<sub>2</sub>H to give D-Me<sub>3</sub>CO<sub>2</sub>CNHCH<sub>2</sub>CO<sub>2</sub>CHPhCO<sub>2</sub>CHPh<sub>2</sub> which was hydrogenolyzed and used to acylate the 7-aminocephem, followed by deblocking, to give I (R = H, R<sub>1</sub> = H<sub>2</sub>NCH<sub>2</sub>CO, R<sub>2</sub> = CH<sub>2</sub>O<sub>2</sub>CCMe<sub>3</sub>, R<sub>3</sub> = 1-methyl-5-tetrazolylthiomethyl, II). At a dose corresponding to 125 mg of the free acid II was 38.0% excreted in the urine in 8 h.

L4 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 1983:59889 CAPLUS

DN 98:59889

TI Improving intestinal absorption of cephalosporin derivatives

IN Nishikido, Joji; Kodama, Eiji; Shibukawa, Mitsuru

PA Asahi Chemical Industry Co., Ltd., Japan

SO Eur. Pat. Appl., 63 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | EP 60422   | A2   | 19820922 | EP 1982-101508  | 19820226 |
|    | EP 60422   | A3   | 19830824 |                 |          |

R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE

|             |    |          |                |          |
|-------------|----|----------|----------------|----------|
|             |    |          | JP 1981-26743  | 19810227 |
|             |    |          | JP 1981-128688 | 19810819 |
| JP 57142988 | A2 | 19820903 | JP 1981-26743  | 19810227 |
| JP 58032885 | A2 | 19830225 | JP 1981-128688 | 19810819 |
| US 4465668  | A  | 19840814 | US 1982-351613 | 19820224 |
|             |    |          | JP 1981-26743  | 19810227 |
|             |    |          | JP 1981-128688 | 19810819 |

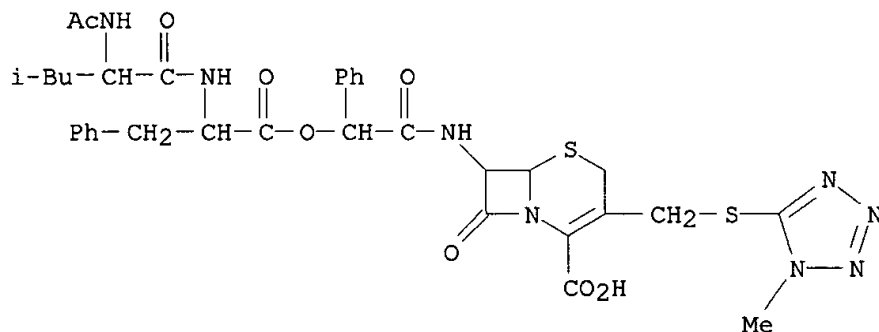
IT 84294-10-0 84330-79-0

RL: PROC (Process)

(absorption of, by intestine)

RN 84294-10-0 CAPLUS

CN L-Phenylalanine, N-(N-acetyl-L-leucyl)-, 2-[[2-carboxy-3-[[[1-methyl-1H-tetrazol-5-yl]thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl]amino]-2-oxo-1-phenylethyl ester, [6R-[6.alpha.,7.beta.(R\*)]]- (9CI)  
(CA INDEX NAME)



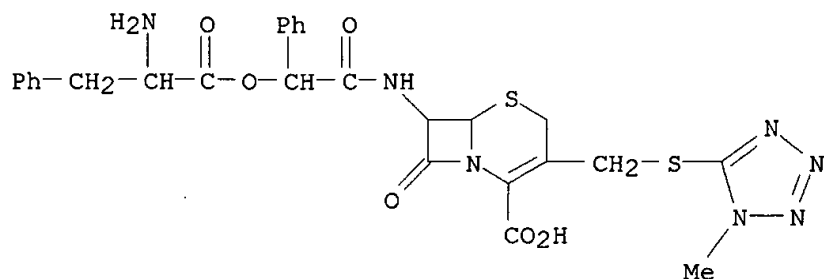
RN 84330-79-0 CAPLUS

CN L-Phenylalanine, 2-[[2-carboxy-3-[[[1-methyl-1H-tetrazol-5-yl]thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl]amino]-2-oxo-1-phenylethyl ester, [6R-[6.alpha.,7.beta.(R\*)]]-, monoformate (9CI) (CA INDEX NAME)

CM 1

CRN 84330-78-9

CMF C27 H27 N7 O6 S2



CM 2

CRN 64-18-6  
CMF C H2 O2

O=CH-OH

IT **84330-75-6P**

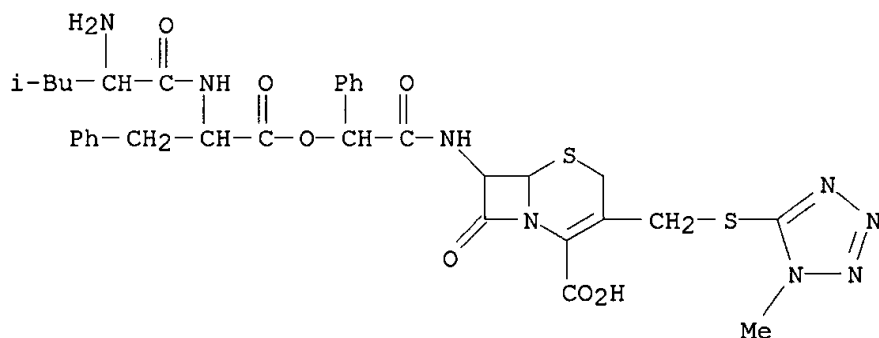
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and intestinal absorption of)

RN 84330-75-6 CAPLUS

CN L-Phenylalanine, N-L-leucyl-, 2-[[2-carboxy-3-[[[1-methyl-1H-tetrazol-5-yl]thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl]amino]-2-oxo-1-phenylethyl ester, [6R-[6.alpha.,7.beta.(R\*)]]-, monoformate (9CI) (CA INDEX NAME)

CM 1

CRN 84330-74-5  
CMF C33 H38 N8 O7 S2

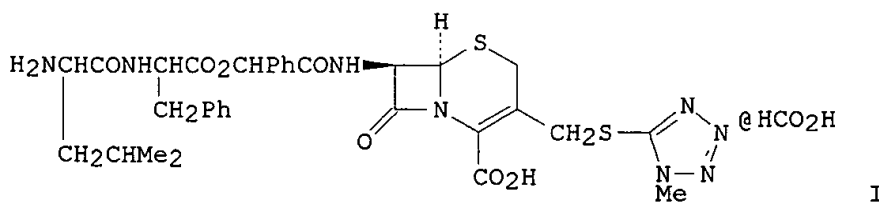


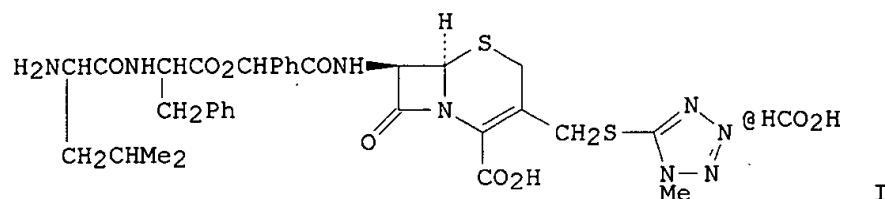
CM 2

CRN 64-18-6  
CMF C H2 O2

O=CH-OH

GI





AB Intestinal absorption of cephalosporins with low oral activity is improved by binding to any side chain in the 3-, 4-, or 7-position of a 7-aminocephalosporanic acid deriv., an oligopeptide  $X(NHCHR_1CO)nNHCHR_2CO$  ( $X = H$ , C1-15 alkyl or  $R_3CO$ ;  $R_1$  and  $R_2$  = side chain of an amino acid constituting the oligopeptide;  $R_3 = H$  or C1-15 alkyl or protective group easily removable by acid hydrolysis, hydrogenolysis, or enzyme existing in a living body;  $n = 1-3$ ). Thus, 7-[D-(O-L-leucyl-L-phenylalanyl)mandelamido]-3-[[1-methyl-1H-tetrazol-5-yl)thio]methyl]-3-cephem-4-carboxylic acid monoformate (I) [84330-75-6] was prepd. and administered to male rats at 50 mg/kg. The blood concn. was 4.51 .mu.g/mL 30 min after administration, as compared with 0.29 .mu.g/mL for the cephemcarboxylic acid deriv. without the oligopeptide.

L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 1981:139710 CAPLUS

DN 94:139710

TI Synthesis of 3,6-alkyl- or aryl-substituted 1,4-oxazine-2,5-diones

AU Irurre Perez, J.; Sanchez Rosell, M.; Travesa Aijon, F.

CS Dep. Quim. Org., Inst. Quim. Sarria, Barcelona, Spain

SO Anales de Quimica, Serie C: Quimica Organica y Bioquimica (1980), 76(1), 47-9

CODEN: AQSBD6; ISSN: 0211-1357

DT Journal

LA Spanish

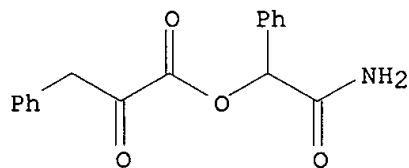
IT 77034-52-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and cyclodehydration of)

RN 77034-52-7 CAPLUS

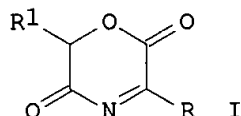
CN Benzenepropanoic acid, .alpha.-oxo-, 2-amino-2-oxo-1-phenylethyl ester, (-)-(9CI) (CA INDEX NAME)

Rotation (-).



GI





AB Oxazinediones I (R = Ph, PhCH<sub>2</sub>, R<sub>1</sub> = Ph; R = p-anisyl, R<sub>1</sub> = Ph, Me) were prepd. by cyclodehydration of RCOCO<sub>2</sub>CHR<sub>1</sub>CONH<sub>2</sub>, which were obtained from RCOCO<sub>2</sub>H and HOCHR<sub>1</sub>CONH<sub>2</sub>. Attempted prepn. of I from HOCHPhCON:CMeco<sub>2</sub>Et resulted only in isomerization to the more stable (E)-isomer.

L4 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 1980:128729 CAPLUS

DN 92:128729

TI Malonic acid derivatives of sterically-hindered piperidines

IN Rody, Jean; Karrer, Friedrich

PA Ciba-Geigy A.-G., Switz.

SO Eur. Pat. Appl., 23 pp.

CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 1

|    | PATENT NO.                    | KIND | DATE     | APPLICATION NO. | DATE     |
|----|-------------------------------|------|----------|-----------------|----------|
| PI | EP 2260                       | A2   | 19790613 | EP 1978-101492  | 19781201 |
|    | EP 2260                       | A3   | 19790627 |                 |          |
|    | EP 2260                       | B1   | 19820714 |                 |          |
|    | R: BE, CH, DE, FR, GB, IT, NL |      |          |                 |          |
|    | JP 54098777                   | A2   | 19790803 | CH 1977-14769   | 19771202 |
|    |                               |      |          | JP 1978-149583  | 19781202 |
|    |                               |      |          | CH 1977-14769   | 19771202 |
|    | US 4237297                    | A    | 19801202 | US 1979-91630   | 19791105 |
|    |                               |      |          | CH 1977-14769   | 19771202 |
|    |                               |      |          | US 1978-963537  | 19781124 |

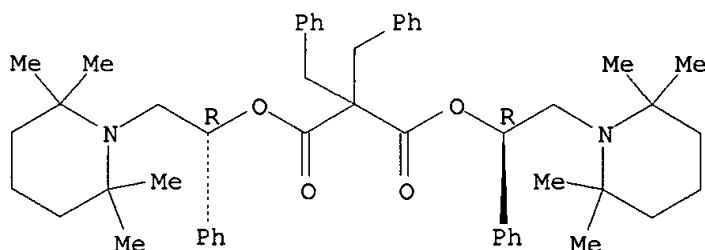
IT 72013-67-3P 72013-73-1P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 72013-67-3 CAPLUS

CN Propanedioic acid, bis(phenylmethyl)-, bis[1-phenyl-2-(2,2,6,6-tetramethyl-1-piperidiny)ethyl] ester, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

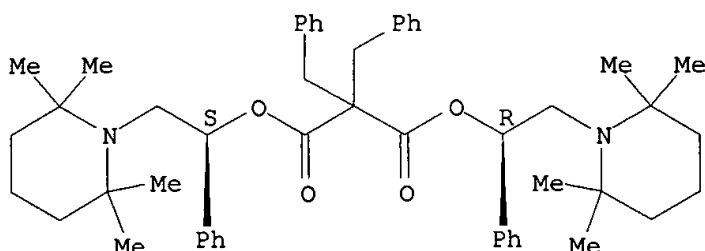


RN 72013-73-1 CAPLUS

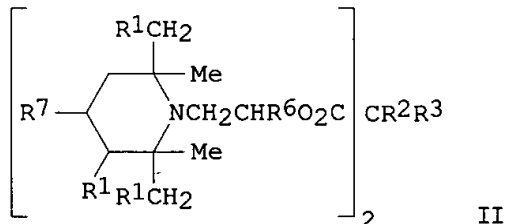
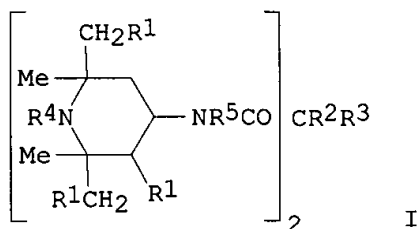
CN Propanedioic acid, bis(phenylmethyl)-, bis[1-phenyl-2-(2,2,6,6-tetramethyl-

1-piperidinyl)ethyl] ester, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



GI



AB The title compds I [R1 = H, lower alkyl; R2 = alkyl, alkenyl, PhCH2; R3 = R2, alkyl- or alkoxyphenyl, CN; R4 = H, OH, aliph. group, PhCH2, (acylated) hydroxyalkyl; R5 = H, (substituted) aliph. group, cycloalkyl, aralkyl, or piperidinyl] or II [R1-R3 = same; R6 = H, Me, Et, Ph; R7 = (etherified) OH, (alkylated) NH2] were prepd. for use as light stabilizers for polymers. Thus, (PhCH2)2C(CO2Me)2 reacted with 1-(2-hydroxyethyl)-2,2,6,6-tetramethylpiperidine and LiNH2 in xylene to give II (R1 = R6 = R7 = H, R2 = R3 = PhCH2).

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 1979:121187 CAPLUS

DN 90:121187

TI Aminoalcohol derivative

IN Lambelin, Georges; Roncucci, Romeo; Roba, Joseph; Gillet, Claude; Snyers, Michel

PA Continental Pharma, Belg.

SO Ger. Offen., 48 pp.

CODEN: GWXXBX  
 DT Patent  
 LA German  
 FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | DE 2817494 | A1   | 19781109 | DE 1978-2817494 | 19780421 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | GB 1603379 | A    | 19811125 | GB 1978-27732   | 19780427 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | GB 1603378 | A    | 19811125 | GB 1978-16813   | 19780427 |
|    |            |      |          | GB 1978-16813   | 19780427 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | SE 7804897 | A    | 19781104 | SE 1978-4897    | 19780428 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | NL 7804621 | A    | 19781107 | NL 1978-4621    | 19780428 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | CA 1118438 | A1   | 19820216 | CA 1978-302239  | 19780428 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | US 4474977 | A    | 19841002 | US 1978-901223  | 19780428 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | IL 54608   | A1   | 19840131 | IL 1978-54608   | 19780501 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | FI 7801347 | A    | 19781104 | FI 1978-1347    | 19780502 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | DK 7801898 | A    | 19781104 | DK 1978-1898    | 19780502 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | NO 7801554 | A    | 19781106 | NO 1978-1554    | 19780502 |
|    | NO 146057  | B    | 19820413 |                 |          |
|    | NO 146057  | C    | 19820721 |                 |          |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | ZA 7802507 | A    | 19790725 | ZA 1978-2507    | 19780502 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    | ES 469843  | A1   | 19790916 | ES 1978-469843  | 19780502 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | AT 7803179 | A    | 19800115 | AT 1978-3179    | 19780502 |
|    | AT 358020  | B    | 19800811 |                 |          |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | FR 2389597 | A1   | 19781201 | FR 1978-13202   | 19780503 |
|    | FR 2389597 | B1   | 19830819 |                 |          |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | AU 7835733 | A1   | 19791108 | AU 1978-35733   | 19780503 |
|    | AU 517255  | B2   | 19810716 |                 |          |
|    |            |      |          | LU 1977-77236   | 19770503 |

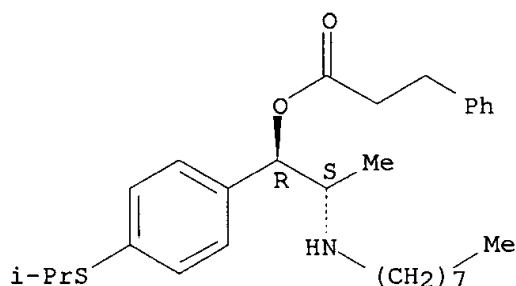
|             |    |          |               |          |
|-------------|----|----------|---------------|----------|
| CH 635570   | A  | 19830415 | LU 1977-77237 | 19770503 |
|             |    |          | CH 1978-4836  | 19780503 |
|             |    |          | LU 1977-77236 | 19770503 |
| JP 53141230 | A2 | 19781208 | LU 1977-77237 | 19770503 |
| JP 59040140 | B4 | 19840928 | JP 1978-53627 | 19780504 |
|             |    |          | LU 1977-77236 | 19770503 |
|             |    |          | LU 1977-77237 | 19770503 |
| AT 7906288  | A  | 19810715 | AT 1979-6288  | 19790925 |
| AT 366023   | B  | 19820310 |               |          |
|             |    |          | LU 1977-77236 | 19770503 |
|             |    |          | LU 1977-77237 | 19770503 |
|             |    |          | AT 1978-3179  | 19780502 |

IT **69145-90-0**RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. as muscle relaxant)

RN 69145-90-0 CAPLUS

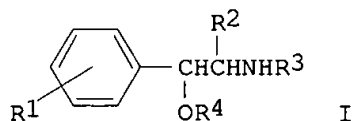
CN Benzenepropanoic acid, 1-[4-[(1-methylethyl)thio]phenyl]-2-(octylamino)propyl ester, hydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

GI



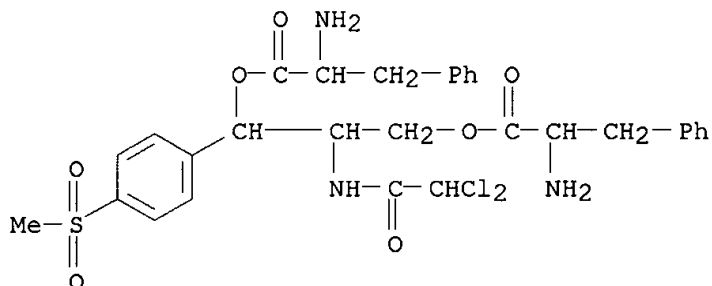
I

AB One hundred three amino alcs. I [R1 = H, C1-5 alkylthio, alkoxy, alkyl, C5-6 cycloalkylthio, cycloalkoxy, cycloalkyl, halo; R2 = C1-3 alkyl; R3 = C1-8 alkyl, C1-4 alkyl, optionally substituted with Ph, PhO, Bz, (un)substituted with alkyl, alkoxy, halo, C6-18 alkenyl, C5-9 cycloalkyl; R4 = COR5 [R5 = C1-10 alkyl, C2-4 alkenyl, C3-8 cycloalkyl, Ph (un)substituted with C1-3 alkyl, alkoxy, halo, C1-4 alkyl, (un)substituted with C1-3 carbalkoxy, alkoxy, NH2, acylamino, C5-6 cycloalkyl, PhO, Ph, optionally substituted with alkyl, alkoxy, halo, cinnamyl], H], useful as antihypertensives, peripheral vasodilators, muscle relaxants, platelet

aggregation inhibitors, hypolipemics, and thrombosis inhibitors, were prepd. Thus, acylation of 4-Me<sub>2</sub>CHSC<sub>6</sub>H<sub>4</sub>CH(OH)CHMeNH(CH<sub>2</sub>)<sub>7</sub>Me by refluxing with AcCl in C<sub>6</sub>H<sub>6</sub> or PrCOCl gave 70 or 52%, resp. of the corresponding 4-Me<sub>2</sub>CHSC<sub>6</sub>H<sub>4</sub>CH(OR<sub>4</sub>)CHMeNH(CH<sub>2</sub>)<sub>7</sub>Me (R<sub>4</sub> = Ac, PrCO).

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2003 ACS  
 AN 1973:147610 CAPLUS  
 DN 78:147610  
 TI Thiamphenicol phenylalaninate  
 IN Saiga, Akisuke; Yamanaka, Motosuke; Sato, Takashi  
 PA Eisai Co., Ltd.  
 SO Jpn. Kokai Tokkyo Koho, 2 pp.  
 CODEN: JKXXAF  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

|    | PATENT NO.  | KIND   | DATE     | APPLICATION NO. | DATE     |
|----|---|--------|----------|-----------------|----------|
| PI | JP 48004446   | B4     | 19730120 | JP 1971-27212   | 19710427 |
| IT | <b>41570-11-0P</b>  |        |          |                 |          |
|    | RL: SPN (Synthetic preparation); PREP (Preparation)<br>(prepn. of)  |        |          |                 |          |
| RN | 41570-11-0  | CAPLUS |          |                 |          |
| CN | L-Phenylalanine, 2-[(dichloroacetyl)amino]-1-[4-(methylsulfonyl)phenyl]-1,3-propanediyl ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME) |        |          |                 |          |



AB A soln. of thiamphenicol and PhCH<sub>2</sub>CH(NH<sub>2</sub>)COCl.HCl (1:2 by mole) in anhyd. dioxane was stirred 7 hr at 13-17.degree. to give 61.2% thiamphenicol phenylalaninate, which was sol. and stable in H<sub>2</sub>O.

L4 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2003 ACS  
 AN 1972:488521 CAPLUS  
 DN 77:88521  
 TI 7-(D-Mandelamido)cephalosporanic acid derivatives  
 IN Berges, David Alan; Dunn, George Lawrence; Hoover, John R. E.  
 PA Smith Kline and French Laboratories  
 SO Ger. Offen., 54 pp.  
 CODEN: GWXXBX  
 DT Patent  
 LA German  
 FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | DE 2158330 | A    | 19720608 | DE 1971-2158330 | 19711124 |

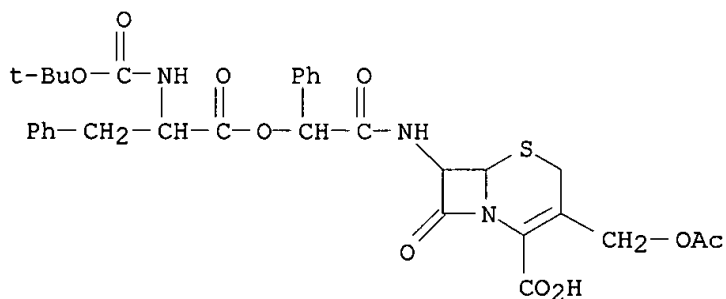
|            |    |          |                |          |
|------------|----|----------|----------------|----------|
| US 3701775 | A  | 19721031 | US 1970-92860  | 19701125 |
| ZA 7107133 | A  | 19720726 | US 1970-92860  | 19701125 |
| CA 960662  | A1 | 19750107 | ZA 1971-7133   | 19711026 |
| BE 775458  | A1 | 19720517 | US 1970-92860  | 19701125 |
| GB 1327510 | A  | 19730822 | CA 1971-126096 | 19711026 |
| CH 567515  | A  | 19751015 | US 1970-92860  | 19701125 |
| FR 2115363 | A5 | 19720707 | BE 1971-110605 | 19711117 |
| FR 2115363 | B1 | 19750613 | US 1970-92860  | 19701125 |
| ES 397308  | A1 | 19740516 | GB 1971-54335  | 19711123 |
| NL 7116207 | A  | 19720529 | US 1970-92860  | 19701125 |
|            |    |          | CH 1971-16996  | 19711123 |
|            |    |          | US 1970-92860  | 19701125 |
|            |    |          | FR 1971-42022  | 19711124 |
|            |    |          | US 1970-92860  | 19701125 |
|            |    |          | ES 1971-397308 | 19711124 |
|            |    |          | US 1970-92860  | 19701125 |
|            |    |          | NL 1971-16207  | 19711125 |
|            |    |          | US 1970-92860  | 19701125 |

IT **37650-89-8P 37650-90-1P 37651-00-6P**  
**37651-01-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

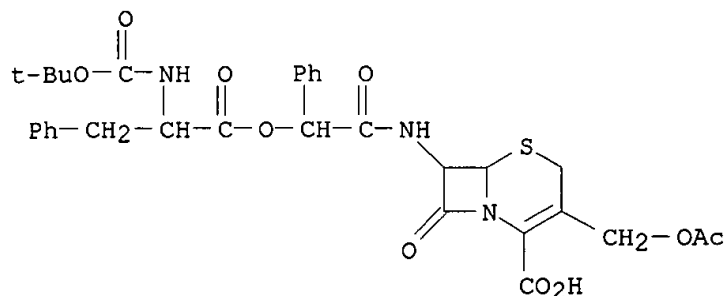
RN 37650-89-8 CAPLUS

CN D-Phenylalanine, N-[(1,1-dimethylethoxy)carbonyl]-, 2-[[3-  
 [(acetyloxy)methyl]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-  
 yl]amino]-2-oxo-1-phenylethyl ester, [6R-[6.alpha.,7.beta.(R\*)]]- (9CI)  
 (CA INDEX NAME)



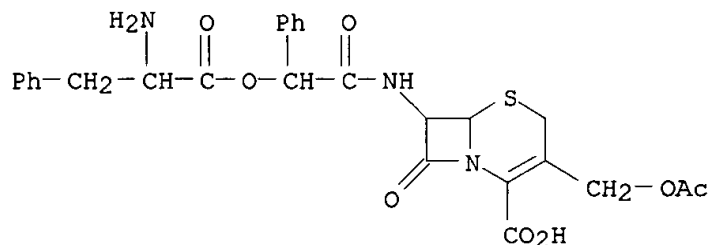
RN 37650-90-1 CAPLUS

CN L-Phenylalanine, N-[(1,1-dimethylethoxy)carbonyl]-, 2-[[3-  
 [(acetyloxy)methyl]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-  
 yl]amino]-2-oxo-1-phenylethyl ester, [6R-[6.alpha.,7.beta.(R\*)]]- (9CI)  
 (CA INDEX NAME)



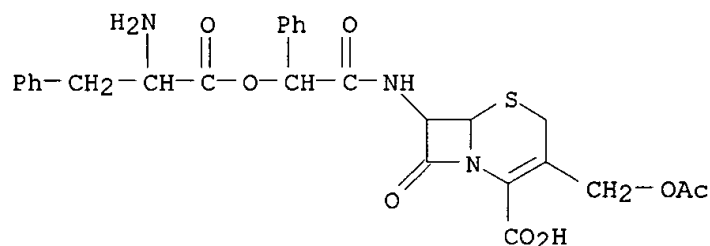
RN 37651-00-6 CAPLUS

CN D-Phenylalanine, 2-[[3-[(acetyloxy)methyl]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl]amino]-2-oxo-1-phenylethyl ester, [6R-[6.alpha.,7.beta.(R\*)]]- (9CI) (CA INDEX NAME)



RN 37651-01-7 CAPLUS

CN L-Phenylalanine, 2-[[3-[(acetyloxy)methyl]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl]amino]-2-oxo-1-phenylethyl ester, [6R-[6.alpha.,7.beta.(R\*)]]- (9CI) (CA INDEX NAME)



AB Fifty-nine title compds. [I, R = e.g., N3CH2CO, H2NCH2CO, Boc-L-methionyl (Boc = Me3CO2C), Boc-D-alanyl, L-methionyl, MeSCH2CO, 2-thenoyl, etc., R1 = e.g., OAc, H, MeO], bactericides, were prepd. via O-acylation of I (R = H) in the presence of N, N -carbonyldiimidazole (II). Thus, II and then I (R = H, R1 = OAc) were added to Boc-methionine in THF, the mixt. was kept 20 hr, and the imidazole salt hydrolyzed to give 50% I (R = Boc-methionyl, R1 = OAc), from which the Boc group was cleaved with CF3CO2H.

L4 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2003 ACS

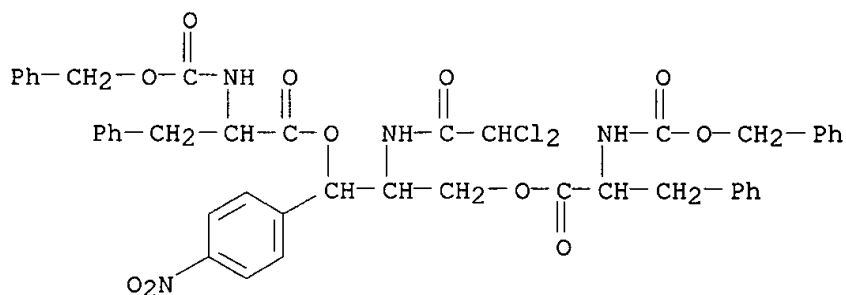
AN 1970:67270 CAPLUS

DN 72:67270

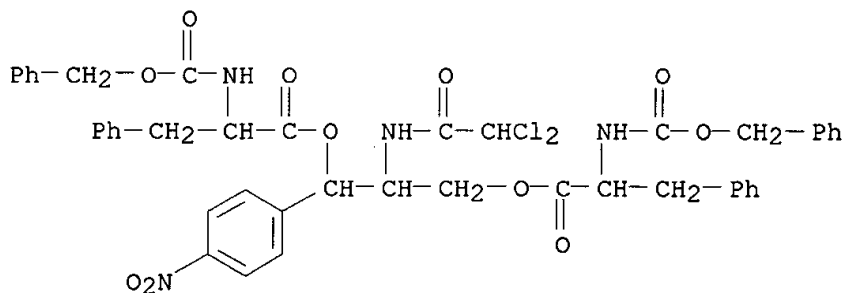
TI Water soluble antibiotic chloramphenicol .beta.-phenylalanine ester salts  
 IN Zumin, Silva T.; Mosna, Sergio  
 PA Pierrel S.p.A.  
 SO Brit., 8 pp.  
 CODEN: BRXXAA  
 DT Patent  
 LA English  
 FAN.CNT 1

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|----|--|------|----------|-----------------|----------|
| PI | GB 1173562   |      | 19691210 | GB              | 19660425 |
| IT | 25613-59-6P 25613-62-1P 25613-63-2P<br>25613-64-3P 25616-21-1P 25616-22-2P |      |          |                 |          |

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 25613-59-6 CAPLUS  
 CN Alanine, N-carboxy-3-phenyl-, N-benzyl ester, L-, diester with  
 D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-  
 nitrophenethyl]acetamide (8CI) (CA INDEX NAME)



RN 25613-62-1 CAPLUS  
 CN Alanine, N-carboxy-3-phenyl-, N-benzyl ester, DL-, diester with  
 D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-  
 nitrophenethyl]acetamide (8CI) (CA INDEX NAME)



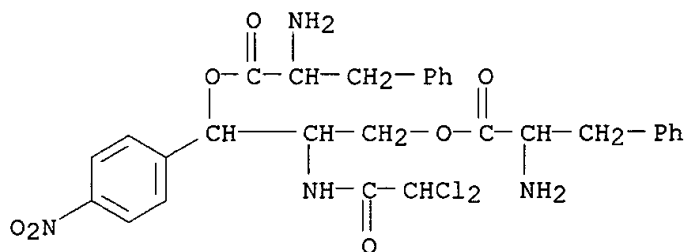
RN 25613-63-2 CAPLUS  
 CN Alanine, phenyl-, L-, diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-  
 .alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide, bis(trifluoroacetate)  
 (8CI) (CA INDEX NAME)

CM 1



CRN 47832-98-4

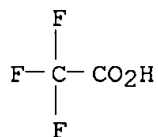
CMF C29 H30 Cl2 N4 O7



CM 2

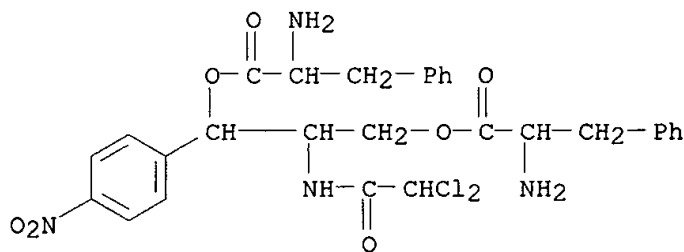
CRN 76-05-1

CMF C2 H F3 O2



RN 25613-64-3 CAPLUS

CN Alanine, phenyl-, L-, diester with D-threo-2,2-dichloro-N-[(beta)-hydroxy-.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide, dihydrochloride (8CI)  
(CA INDEX NAME)



● 2 HCl

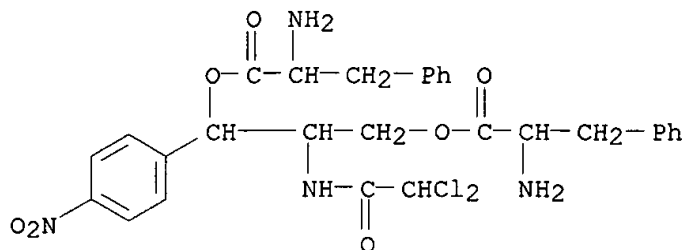
RN 25616-21-1 CAPLUS

CN Alanine, N-acetyl-3-phenyl-, L-, compd. with L-phenylalanine diester with D-threo-2,2-dichloro-N-[(beta)-hydroxy-.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide (2:1) (8CI) (CA INDEX NAME)

CM 1

CRN 47832-98-4

CMF C29 H30 Cl2 N4 O7

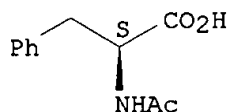


CM 2

CRN 2018-61-3

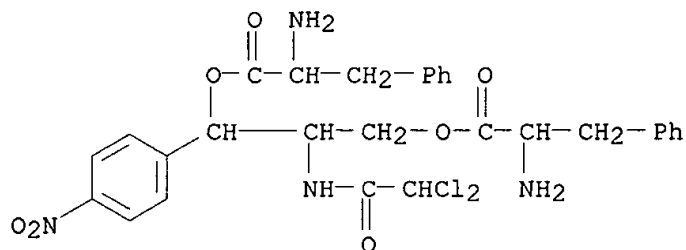
CMF C11 H13 N O3

Absolute stereochemistry. Rotation (+).



RN 25616-22-2 CAPLUS

CN Alanine, phenyl-, DL-, diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide, dihydrobromide (8CI)  
(CA INDEX NAME)

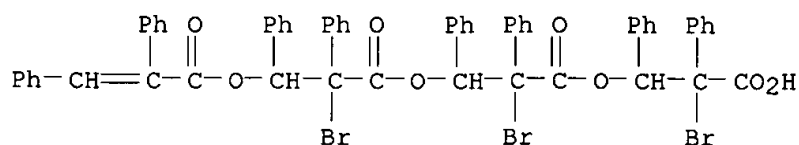


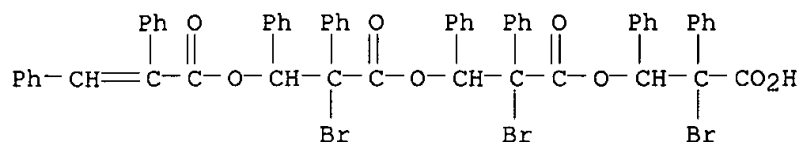
● 2 HBr

AB Salts of chloramphenicol 1,3-bis(L-.beta.-phenylalaninate) (I) and chloramphenicol 3-L-.beta.-phenylalaninate (II), useful for parenteral administration, with antibiotic activity, were prepd. by reacting D-(-)-threo-1-p-nitrophenyl-2-dichloroacetamido-1,3-propanediol (chloramphenicol) (III) either with N-carbobenzoxy-L-.beta.-phenylalanine (IV) in the presence of dicyclo-hexylcarbodiimide (V) and anhyd. pyridine

(VI) or with IV anhydride (VII) in the presence of VI to give chloramphenicol 1,3-bis(N-carbobenzoxy-L-.beta.-phenylalaninate) (VIII) and chloramphenicol 3-(N-carbobenzoxy-L-.beta.-phenylalaninate) (IX), resp., followed by removal of the protecting group(s) by treatment with aq. HBr or anhyd. CF<sub>3</sub>CO<sub>2</sub>H. I and II are hydrolyzed in vivo to III and phenylalanine. Thus, addn. of 10.30 g V at 15.degree. to a stirred soln. of 29.93 g IV in 150 ml Me<sub>2</sub>CO, and the mixt. stirred 3 hr gave 96.5% VII. Racemic N-carbobenzoxy-DL-.beta.-phenylalanine anhydride (X) (93.5%) was prepd. similarly. III (5.82 g) in 10 ml VI was added to 180 ml of an Me<sub>2</sub>CO soln. of 25.2 g VII and the mixt. stirred 5-6 hr at room temp. and poured on ice-HCl to give, after treatment with 3.5 ml p-H<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>NMe<sub>2</sub> (XI) in dry C<sub>6</sub>H<sub>6</sub> to remove excess VII, 90% VIII, m. 95-7.degree.. Racemic chloramphenicol 1,3-bis(N-carbobenzoxy-.beta.-phenylalaninate) (XII) (94%), a yellow oil, was prepd. similarly from X. IV (22.45 g) and 15 ml VI added to a stirred soln. of 9.69 g III in 60 ml HCONMe<sub>2</sub>, the soln. cooled to -5 to -8.degree., 18.57 g V added slowly, the mixt. stirred 1 hr, kept 3 hr at -5.degree. and poured on a mixt. of 50 ml concd. HCl, 50 ml H<sub>2</sub>O, and 100 g ice gave a ppt., which was centrifuged off and extd. with C<sub>6</sub>H<sub>6</sub>. Treatment of the C<sub>6</sub>H<sub>6</sub> ext. with 3.5 ml XI gave 93% VIII, m. 95-7.degree.. IX, m. 145-7.degree., was prepd. similarly using 19.39 g III, 60 ml HCONMe<sub>2</sub>, 17.96 g IV, 15 ml VI, and 12.38 g V. A mixt. of 17.72 g VIII and 40 ml anhyd. CF<sub>3</sub>CO<sub>2</sub>H refluxed 1 hr in the presence of 8 g resorcinol gave 16.30 g I.CF<sub>3</sub>CO<sub>2</sub>H (XIII). Addn. of XIII to satd. aq. NaHCO<sub>3</sub>, extn. of the free base with CH<sub>2</sub>Cl<sub>2</sub>, and treatment of the ext. with HCl gave I.HCl, m. 220-222.degree. (decompn.). II.HCl, [.alpha.]<sub>D</sub><sup>20</sup> 10.77.degree. (c 2, H<sub>2</sub>O), was prepd. similarly from IX. A soln. of 5 g XII in 60 ml 2.5N HBr in AcOH stirred 10 min at 25 .degree. gave 85% a mixt. of chloramphenicol 1,3-bis(D- and L-.beta.-phenylalaninate-HBr) sepd. by chromatog. XIII (13 g) treated with satd. aq. NaHCO<sub>3</sub>, extn. of the free base with CH<sub>2</sub>Cl<sub>2</sub>, and treatment of the ext. with N-acetyl-L-phenylalanine gave III 1,3-bis(L-.beta.-phenylalaninate N-acetyl-L-phenylalaninate); III 3-(L-.beta.-phenylalaninate N-acetyl-L-phenylalaninate) was prepd. similarly.

L4 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2003 ACS  
 AN 1969:470266 CAPLUS  
 DN 71:70266  
 TI Bromination of silver and sodium stilbenecarboxylates  
 AU Price, Charles C.; Blunt, Harry W.  
 CS Univ. of Pennsylvania, Philadelphia, PA, USA  
 SO Journal of Organic Chemistry (1969), 34(8), 2484-6  
 CODEN: JOCEAH; ISSN: 0022-3263  
 DT Journal  
 LA English  
 IT **19926-35-3P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 19926-35-3 CAPLUS  
 CN Acrylic acid, 2,3-diphenyl-, ester with 2-bromo-2,3-diphenylhydracrylic acid trimol. ester (8CI) (CA INDEX NAME)





AB The ag salts of cis-PhCH:C(CO<sub>2</sub>H)Ph (cis-I) and trans-I are treated with Br to give mixts. of .alpha.-bromo-.alpha.,.beta.-diphenyl-.beta.-propiolactone (II), a macrocyclic polymer (III), and a linear polymer; II is dissolved in MeOH to give III. cis-I Na salt gives a .beta.-lactone (IV), cis-PhCH:CB<sub>r</sub>Ph, and PhCH<sub>2</sub>COPh (V); V is obtained from trans-I Na salt. It is proposed that IV is a geometrical isomer of II. IV does not give a polymer.

L4 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2003 ACS

AN 1967:402830 CAPLUS

DN 67:2830

TI Separation of the organic bases by Craig partition. VII. Acyl migration in the stereoisomeric N-(N,N-dimethylphenylalanyl)ephedrine

AU Schoenenberger, Helmut; Fuchsberger, K. D.; Brinkmann, Rolf

CS Univ. Munich, Munich, Fed. Rep. Ger.

SO Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft (1967), 300(2), 126-35

CODEN: APBDAJ; ISSN: 0376-0367

DT Journal

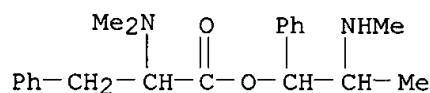
LA German

IT 14355-01-2P 14355-02-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 14355-01-2 CAPLUS

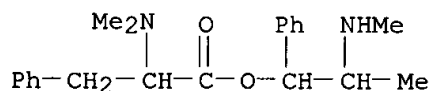
CN Alanine, N,N-dimethyl-3-phenyl-, ester with (-)-pseudoephedrine, dihydrochloride, L- (8CI) (CA INDEX NAME)



● 2 HCl

RN 14355-02-3 CAPLUS

CN Alanine, N,N-dimethyl-3-phenyl-, ester with (-)-pseudoephedrine, dihydrochloride, D- (8CI) (CA INDEX NAME)



2 HCl

AB cf. CA 66: 49281u. The compds. studied were N-(L-N,N-dimethylphenylalanyl)-L-ephedrine (I), N-(D-N,N-dimethylphenylalanyl)-L-ephedrine (II), N-(L-N,N-dimethylphenylalanyl)-L-pseudoephedrine (III), and N-(D-N,N-dimethylphenylalanyl)-L-pseudoephedrine (IV). In every case, only the ester of L-pseudoephedrine resulted, even under mild conditions (room temp., acetone-HCl). Complete inversion of the erythro derivs. occurred. In 2N HCl at 80.degree., the ester from I formed quant. in 10 min. while that from III (retention of configuration) required 25 hrs. With II, 5 hrs. and with IV, 22 hrs. were required. The 4 amides pass through either of 2 cyclic intermediates during the migration, L,L-(V) or D,L-pseudooxazolidine (VI). The rates are explained by steric considerations of the mechanism, V resulting from I via inversion and from III with retention, and VI, from II via inversion and IV with retention. Craig partition as described previously (loc. cit.) was used to sep. and det. the reaction products. Twenty-four partition steps using a solvent mixt. of 0.5M citrate buffer (pH 4/5)-MeOH-CHCl<sub>3</sub> (9:1:10 parts by vol.) were required for sepn. into N- and O-aminoacylephedrines. The O-(L-N,N-dimethylphenylalanyl)-L-pseudoephedrine m. 170-2.degree., [.alpha.]<sub>20D</sub> + 114.degree. (c = 0.0055 g./ml., 5N HCl) and the O-(D-N,N-dimethyl-) ester melts at 174-6.degree., [.alpha.]<sub>20D</sub> 48.degree. (c 0.0055 g./ml., 5N HCl).

=> d cost

COST IN U.S. DOLLARS

| SINCE FILE | TOTAL   |
|------------|---------|
| ENTRY      | SESSION |
| 0.34       | 0.83    |
| 0.06       | 0.18    |
| 0.00       | 147.75  |
| 100.79     | 100.79  |
| -----      | -----   |
| 101.19     | 249.55  |
| 5.06       | 5.06    |
| -----      | -----   |
| 106.25     | 254.61  |

CAPLUS FEE (5%)

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

| SINCE FILE | TOTAL   |
|------------|---------|
| ENTRY      | SESSION |
| -14.32     | -14.32  |

IN FILE 'CAPLUS' AT 14:30:48 ON 26 MAY 2003

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LOGINID:sssptal611sxp

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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| NEWS | 2  | Apr 08 | "Ask CAS" for self-help around the clock  |
| NEWS | 3  | Jun 03 | New e-mail delivery for search results now available  |
| NEWS | 4  | Aug 08 | PHARMAMarketLetter(PHARMAML) - new on STN   |
| NEWS | 5  | Aug 19 | Aquatic Toxicity Information Retrieval (AQUIRE)<br>now available on STN                       |
| NEWS | 6  | Aug 26 | Sequence searching in REGISTRY enhanced   |
| NEWS | 7  | Sep 03 | JAPIO has been reloaded and enhanced  |
| NEWS | 8  | Sep 16 | Experimental properties added to the REGISTRY file  |
| NEWS | 9  | Sep 16 | CA Section Thesaurus available in CAPLUS and CA   |
| NEWS | 10 | Oct 01 | CASREACT Enriched with Reactions from 1907 to 1985  |
| NEWS | 11 | Oct 24 | BEILSTEIN adds new search fields  |
| NEWS | 12 | Oct 24 | Nutraceuticals International (NUTRACEUT) now available on STN                                 |
| NEWS | 13 | Nov 18 | DKILIT has been renamed APOLLIT   |
| NEWS | 14 | Nov 25 | More calculated properties added to REGISTRY  |
| NEWS | 15 | Dec 04 | CSA files on STN  |
| NEWS | 16 | Dec 17 | PCTFULL now covers WP/PCT Applications from 1978 to date                                      |
| NEWS | 17 | Dec 17 | TOXCENTER enhanced with additional content  |
| NEWS | 18 | Dec 17 | Adis Clinical Trials Insight now available on STN   |
| NEWS | 19 | Jan 29 | Simultaneous left and right truncation added to COMPENDEX,<br>ENERGY, INSPEC                  |
| NEWS | 20 | Feb 13 | CANCERLIT is no longer being updated  |
| NEWS | 21 | Feb 24 | METADEx enhancements  |
| NEWS | 22 | Feb 24 | PCTGEN now available on STN   |
| NEWS | 23 | Feb 24 | TEMA now available on STN   |
| NEWS | 24 | Feb 26 | NTIS now allows simultaneous left and right truncation  |
| NEWS | 25 | Feb 26 | PCTFULL now contains images   |
| NEWS | 26 | Mar 04 | SDI PACKAGE for monthly delivery of multifile SDI results                                     |
| NEWS | 27 | Mar 20 | EVENTLINE will be removed from STN  |
| NEWS | 28 | Mar 24 | PATDPAFULL now available on STN   |
| NEWS | 29 | Mar 24 | Additional information for trade-named substances without<br>structures available in REGISTRY |
| NEWS | 30 | Apr 11 | Display formats in DGENE enhanced   |
| NEWS | 31 | Apr 14 | MEDLINE Reload  |
| NEWS | 32 | Apr 17 | Polymer searching in REGISTRY enhanced  |
| NEWS | 33 | Apr 21 | Indexing from 1947 to 1956 being added to records in CA/CAPLUS                                |
| NEWS | 34 | Apr 21 | New current-awareness alert (SDI) frequency in<br>WPIDS/WPINDEX/WPIX                          |
| NEWS | 35 | Apr 28 | RDISCLOSURE now available on STN  |
| NEWS | 36 | May 05 | Pharmacokinetic information and systematic chemical names<br>added to PHAR                    |
| NEWS | 37 | May 15 | MEDLINE file segment of TOXCENTER reloaded  |
| NEWS | 38 | May 15 | Supporter information for ENCOMPPAT and ENCOMPLIT updated                                     |
| NEWS | 39 | May 16 | CHEMREACT will be removed from STN  |

NEWS 40 May 19 Simultaneous left and right truncation added to WSCA  
NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and  
right truncation

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT  
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),  
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003  
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NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
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FILE 'HOME' ENTERED AT 14:37:32 ON 26 MAY 2003

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 14:37:43 ON 26 MAY 2003

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STRUCTURE FILE UPDATES: 25 MAY 2003 HIGHEST RN 519753-05-0

DICTIONARY FILE UPDATES: 25 MAY 2003 HIGHEST RN 519753-05-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNote 27, Searching Properties  
in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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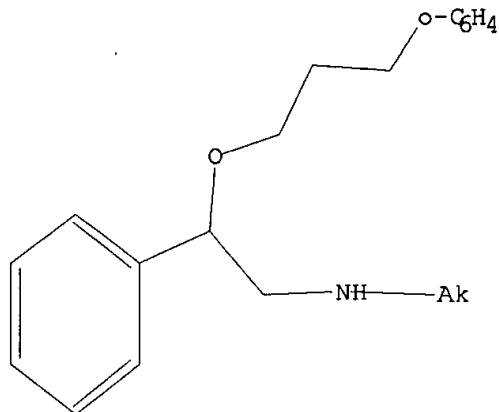
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L1 STRUCTURE UPLOADED

=&gt; d l1

L1 HAS NO ANSWERS

L1 STR



G1 NH,X,Hy

Structure attributes must be viewed using STN Express query preparation.

=&gt; s l1

SAMPLE SEARCH INITIATED 14:38:06 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1045 TO ITERATE

95.7% PROCESSED 1000 ITERATIONS  
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)  
SEARCH TIME: 00.00.01

1 ANSWERS

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 18961 TO 22839

PROJECTED ANSWERS: 1 TO 81

L2 1 SEA SSS SAM L1

=&gt; s l1 sss full

FULL SEARCH INITIATED 14:38:13 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 20951 TO ITERATE

100.0% PROCESSED 20951 ITERATIONS  
SEARCH TIME: 00.00.01

24 ANSWERS

L3 24 SEA SSS FUL L1

=&gt; file caplus

COST IN U.S. DOLLARS

SINCE FILE  
ENTRY

TOTAL  
SESSION

FULL ESTIMATED COST

148.15

148.36

FILE 'CAPLUS' ENTERED AT 14:38:21 ON 26 MAY 2003



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FILE COVERS 1907 - 26 May 2003 VOL 138 ISS 22  
FILE LAST UPDATED: 25 May 2003 (20030525/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

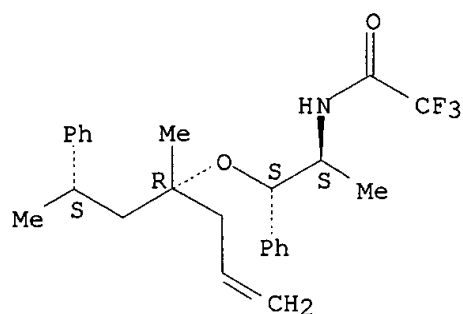
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L4 10 L3

=> d l4 fbib hitstr abs total

L4 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2003 ACS  
AN 2001:57805 CAPLUS  
DN 134:252075  
TI Synthesis of enantiopure homoallylic ethers by reagent controlled facial selective allylation of chiral ketones  
AU Tietze, Lutz F.; Weigand, Berthold; Volkel, Ludwig; Wulff, Christian; Bittner, Christian  
CS Institut fur Organische Chemie Georg-August-Universitat Gottingen, Gottingen, 37077, Germany  
SO Chemistry--A European Journal (2001), 7(1), 161-168  
CODEN: CEUJED; ISSN: 0947-6539  
PB Wiley-VCH Verlag GmbH  
DT Journal  
LA English  
OS CASREACT 134:252075  
IT **330798-68-0P 330798-69-1P**  
RL: BYP (Byproduct); SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of enantiopure homoallylic ethers by reagent controlled facial selective allylation of chiral ketones)  
RN 330798-68-0 CAPLUS  
CN Acetamide, 2,2,2-trifluoro-N-[(1S,2S)-1-methyl-2-[[[(1R)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

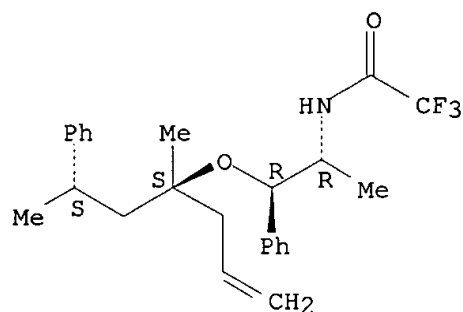
Absolute stereochemistry.



RN 330798-69-1 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[[(1S)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

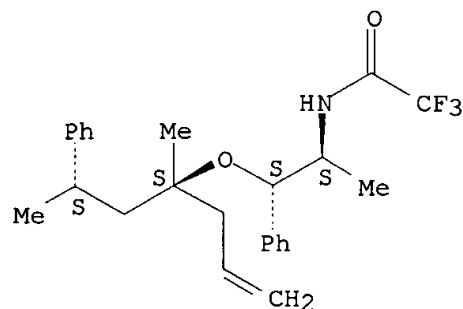
Absolute stereochemistry.

IT 330798-62-4P 330798-63-5P 330798-73-7P  
330798-76-0PRL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of enantiopure homoallylic ethers by reagent controlled  
facial selective allylation of chiral ketones)

RN 330798-62-4 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1S,2S)-1-methyl-2-[[[(1S)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

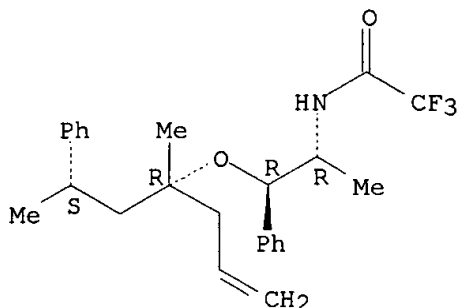
Absolute stereochemistry. Rotation (-).



RN 330798-63-5 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1R)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

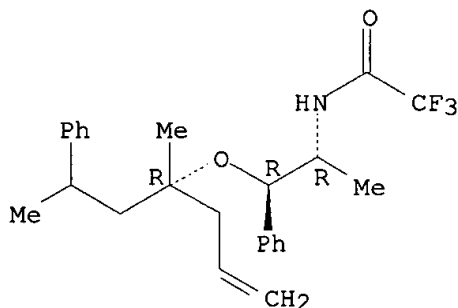
Absolute stereochemistry. Rotation (+).



RN 330798-73-7 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1R)-1-methyl-1-(2-phenylpropyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

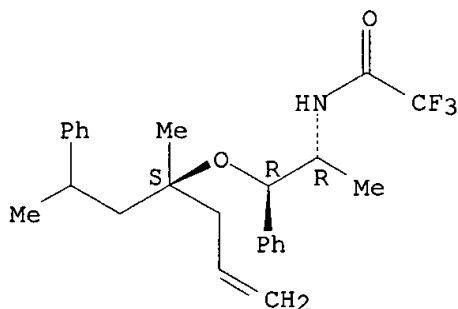
Absolute stereochemistry.



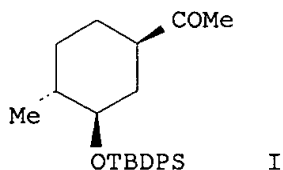
RN 330798-76-0 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1S)-1-methyl-1-(2-phenylpropyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB The stereoselective allylation of chiral Me ketones to give tertiary homoallylic ethers, which can easily be transformed into homoallylic alcs., is described. Reaction of the enantiopure ketones (I), (R)-Me<sub>2</sub>CH(CH<sub>2</sub>)<sub>3</sub>CH(.beta.Me)CH<sub>2</sub>COMe, (R)-MeCH(.beta.OSiPh<sub>2</sub>CMe<sub>3</sub>)CH<sub>2</sub>COMe, (S)-MeCH(.alpha.Ph)CH<sub>2</sub>COMe and the racemic ketones MeCH(OSiPh<sub>2</sub>CMe<sub>3</sub>)CH<sub>2</sub>COMe, MeCH(Ph)CH<sub>2</sub>COMe, MeCH<sub>2</sub>CH(Ph)COMe, MeCH<sub>2</sub>CH(Me)COMe with the norpseudoephedrine deriv. and allylsilane in the presence of a catalytic amt. of trifluoromethanesulfonic acid, led to a series of homoallylic ethers with good to excellent diastereoselectivity (85:15 to > 97:3). The allylation is reagent controlled and nearly independent from the stereogenic centers in the substrates. A partial kinetic resolu. was obsd. using the racemic ketones. In the reaction of the chiral ketones with the achiral reagents ethoxytrimethylsilane and allylsilane only a low diastereoselectivity was obsd.

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1998:625620 CAPLUS

DN 129:316000

TI Synthesis of enantiopure homoallylic alcohols by a highly selective asymmetric allylation of ketones

AU Tietze, Lutz F.; Schiemann, Kai; Wegner, Christoph; Wulff, Christian

CS Institute Organic Chemistry, Georg-August-Universitat Gottingen, Gottingen, D-37077, Germany

SO Chemistry--A European Journal (1998), 4(9), 1862-1869

CODEN: CEUJED; ISSN: 0947-6539

PB Wiley-VCH Verlag GmbH

DT Journal

LA English

OS CASREACT 129:316000

IT 165823-95-0P

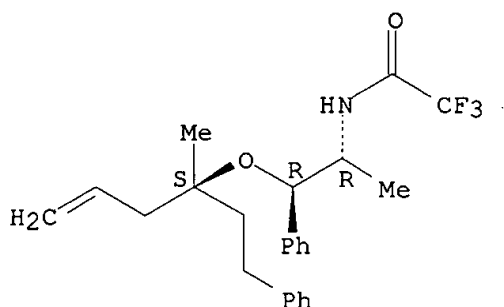
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of enantiopure homoallylic alcs. by asym. allylation of ketones)

RN 165823-95-0 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[[(1S)-1-methyl-1-(2-phenylethyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB A highly selective asym. domino allylation of aliph. ketones is described. When Me ketones, (R,R)-Me<sub>2</sub>SiOCHPhCHMeNHCOCF<sub>3</sub>, and CH<sub>2</sub>:CHCH<sub>2</sub>SiMe<sub>3</sub> react in the presence of catalytic amts. of trifluoromethanesulfonic acid, the homoallylic ethers are produced with up to 24:1 diastereoselectivity and 89% yield. Ether cleavage using lithium or sodium in liq. ammonia gives the homoallylic alcs. in 75 to 95% yield and up to 92% ee. Even EtCOMe, the most difficult example, showed a stereoselectivity of 9:1 at -78.degree.C and 24:1 at -109.degree.C. In addn., the allylation of protected hydroxyalkyl Me ketones gave the corresponding homoallylic ethers with a diastereoselectivity of up to >244:1 and 98% yield. In contrast, Et alkyl ketones have a low selectivity.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1997:639948 CAPLUS

DN 127:307269

TI Preparation of optically active succinic acid derivatives. I. Optical resolution of 2-benzyl-3-(cis-hexahydroisoindolin-2-ylcarbonyl)propionic acid

AU Yamaguchi, Toshiaki; Yanagi, Takashi; Hokari, Hiroshi; Mukaiyama, Yuko; Kamijo, Tetsuhide; Yamamoto, Iwao

CS Kissei Pharmaceutical Co., Ltd., Central Research Laboratories, Hotaka, 399-83, Japan

SO Chemical & Pharmaceutical Bulletin (1997), 45(9), 1518-1520

CODEN: CPBTAL; ISSN: 0009-2363

PB Pharmaceutical Society of Japan

DT Journal

LA English

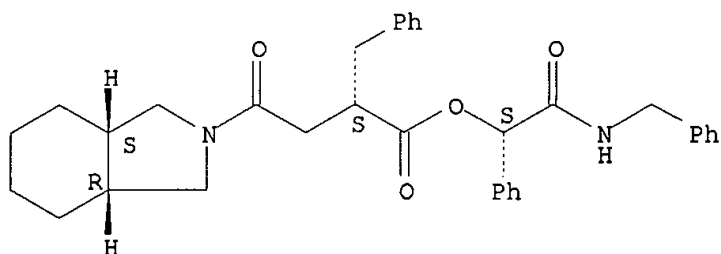
IT 197447-44-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(optical resolu. of benzyl(hexahydroisoindoliny)carbonyl)propionic acid)

RN 197447-44-2 CAPLUS

CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, 2-oxo-1-phenyl-2-[(phenylmethyl)amino]ethyl ester, [2(.alpha.S)-[2[R\*(R\*)],3a.alpha.,7a.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



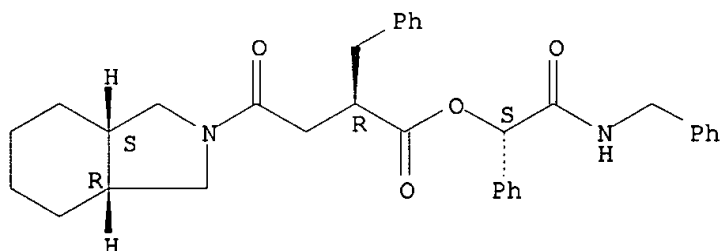
IT 197447-45-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(optical resolu. of benzyl(hexahydroisoindolinylcarbonyl)propionic acid)

RN 197447-45-3 CAPLUS

CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-  
, 2-oxo-1-phenyl-2-[(phenylmethyl)amino]ethyl ester, [2(.alpha.R)-  
[2[R\*(S\*)],3a.alpha.,7a.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB Optical resolu. of 2-benzyl-3-(cis-hexahydroisoindolin-2-ylcarbonyl)propionic acid (I) was accomplished by two methods. Thus, I was esterified with (S)-N-benzylmandelamide and the resulting diastereomeric esters were sepd. by column chromatog. on silica gel. One of the diastereomers was hydrolyzed to give the optically active acid (-)-I. The abs. configuration of (-)-I was established as S by comparison with an authentic sample. The alternative method was resolu. using an optically active amine. Treatment of a soln. of the racemic acid I with 0.65 equiv of (R)-1-(1-naphthyl)ethylamine in ethanol gave the salt in 23.2% yield with an optical purity of 96.8% ee.

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1995:835557 CAPLUS

DN 123:256542

TI Preparation of annelated dihydropyridines

IN Roos, Otto; Loesel, Walter; Arndts, Dietrich

PA Boehringer Ingelheim KG, Germany

SO Ger. Offen., 28 pp.

CODEN: GWXXBX

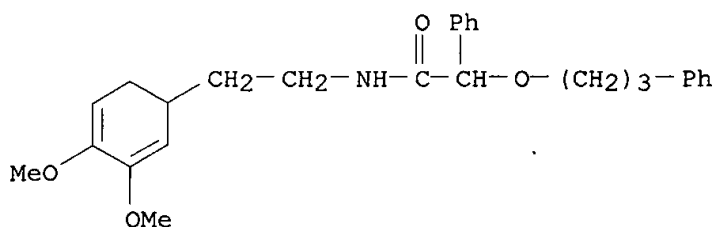
DT Patent

LA German

FAN.CNT 1

| PATENT NO. | KIND  | DATE  | APPLICATION NO. | DATE  |
|------------|-------|-------|-----------------|-------|
| _____      | _____ | _____ | _____           | _____ |

|    |  |    |          |                    |          |
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| PI | DE 4343683   | A1 | 19950622 | DE 1993-4343683    | 19931221 |
|    | CA 2178209   | AA | 19950629 | CA 1994-2178209    | 19941214 |
|    |  |    |          | DE 1993-4343683A   | 19931221 |
|    | WO 9517389   | A1 | 19950629 | WO 1994-EP4150     | 19941214 |
|    | W: AU, CA, CN, JP, KR, PL, RU  |    |          |                    |          |
|    | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE   |    |          |                    |          |
|    |  |    |          | DE 1993-4343683A   | 19931221 |
|    | AU 9512433   | A1 | 19950710 | AU 1995-12433      | 19941214 |
|    | AU 699208  | B2 | 19981126 |                    |          |
|    |  |    |          | DE 1993-4343683A   | 19931221 |
|    |  |    |          | WO 1994-EP4150 W   | 19941214 |
|    | EP 736011  | A1 | 19961009 | EP 1995-903342     | 19941214 |
|    | EP 736011  | B1 | 20000726 |                    |          |
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|    |  |    |          | WO 1994-EP4150 W   | 19941214 |
|    | CN 1138325   | A  | 19961218 | CN 1994-194572     | 19941214 |
|    | CN 1044905   | B  | 19990901 |                    |          |
|    |  |    |          | DE 1993-4343683A   | 19931221 |
|    | JP 09506882  | T2 | 19970708 | JP 1994-517154     | 19941214 |
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|    |  |    |          | WO 1994-EP4150 W   | 19941214 |
|    | RU 2136664   | C1 | 19990910 | RU 1996-115153     | 19941214 |
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|    |  |    |          | WO 1994-EP4150 W   | 19941214 |
|    | AT 194978  | E  | 20000815 | AT 1995-903342     | 19941214 |
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|    |  |    |          | WO 1994-EP4150 W   | 19941214 |
|    | ES 2149958   | T3 | 20001116 | ES 1995-903342     | 19941214 |
|    |  |    |          | DE 1993-4343683A   | 19931221 |
|    | ZA 9410115   | A  | 19950621 | ZA 1994-10115      | 19941220 |
|    |  |    |          | DE 1993-4343683A   | 19931221 |
|    | US 5661157   | A  | 19970826 | US 1994-360867     | 19941221 |
|    |  |    |          | DE 1993-4343683A   | 19931221 |
|    | TW 404941  | B  | 20000911 | TW 1994-83112295   | 19941228 |
|    |  |    |          | DE 1993-4343683A   | 19931221 |
|    | US 5968948   | A  | 19991019 | US 1997-857643     | 19970516 |
|    |  |    |          | DE 1993-4343683A   | 19931221 |
|    |  |    |          | US 1994-360867 A31 | 19941221 |
|    | US 6136819   | A  | 20001024 | US 1999-329443     | 19990610 |
|    |  |    |          | DE 1993-4343683A   | 19931221 |
|    |  |    |          | US 1994-360867 A31 | 19941221 |
|    |  |    |          | US 1997-857643 A31 | 19970516 |
| OS | MARPAT 123:256542  |    |          |                    |          |
| IT | <b>168545-16-2P</b>  |    |          |                    |          |
|    | RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  |    |          |                    |          |
|    | (Reactant or reagent)  |    |          |                    |          |
|    | (prepn. of annelated dihydropyridines from)  |    |          |                    |          |
| RN | 168545-16-2 CAPLUS   |    |          |                    |          |
| CN | Benzeneacetamide, N-[2-(3,4-dimethoxy-2,4-cyclohexadien-1-yl)ethyl]-<br>.alpha.-(3-phenylpropoxy)- (9CI) (CA INDEX NAME) |    |          |                    |          |



GI For diagram(s), see printed CA Issue.

AB The title compds. [I; A = benzo, thieno, indolo; B = O, S, (un)substituted CH<sub>2</sub>; R<sub>2</sub> = OH, alkoxy, benzyloxy, halogen, alkyl, methanesulfonyloxy, etc.; R<sub>3</sub> = 2- or 3-thienyl, (un)substituted Ph, alkyl, cycloalkylalkyl; R<sub>4</sub> = (un)branched alkenyl or alkynyl, alkoxy, dialkylamino, heterocyclyl, Ph, etc.; m = 0-3] (e.g., II), useful as calcium-channel blockers (no data), are prepd. by the intramol. cyclocondensation of arom. amides (III) (e.g., IV) in the presence of condensing agents (e.g., POCl<sub>3</sub>), and I-contg. formulations are also presented.

L4 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1995:568922 CAPLUS

DN 123:111518

TI Enantioselective Synthesis of Tertiary Homoallylic Alcohols via Diastereoselective Addition of Allylsilanes to Ketones

AU Tietze, Lutz F.; Schiemann, Kai; Wegner, Christoph

CS Institute of Organic Chemistry, Georg-August-Universitaet, Goettingen, D-37077, Germany

SO Journal of the American Chemical Society (1995), 117(21), 5851-2

CODEN: JACSAT; ISSN: 0002-7863

PB American Chemical Society

DT Journal

LA English

OS CASREACT 123:111518

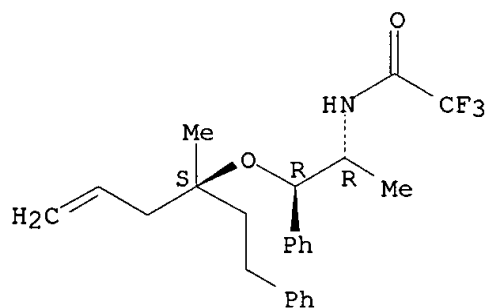
IT 165823-95-0P 166021-67-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(enantioselective synthesis of tertiary homoallylic alcs. via diastereoselective addn. of allylsilanes to ketones)

RN 165823-95-0 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1S)-1-methyl-1-(2-phenylethyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

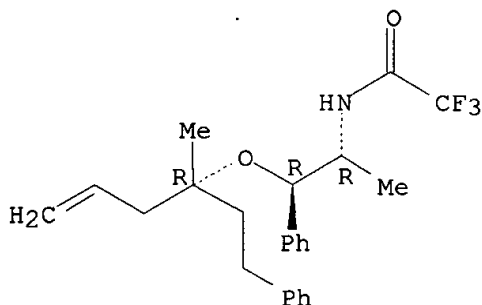




RN 166021-67-6 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[1-methyl-2-[[1-methyl-1-(2-phenylethyl)-3-butenyl]oxy]-2-phenylethyl]-, {1R-[1R\*,2R\*(R\*)]}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Enantiopure tertiary homoallylic alcs.  $\text{CH}_2:\text{CHCH}_2\text{CRMeOH}$  ( $\text{R} = \text{alkyl}$ ) can be obtained from the corresponding homoallylic ethers  $\text{CH}_2:\text{CHCH}_2\text{CRMeOR}_1$  [4,  $\text{R}_1 = \text{residue of (1R,2R)-N-(trifluoroacetyl)norpseudoephedrine}$ ] by treatment with sodium in liq. ammonia. The ethers 4 are formed highly selectively by treatment of the ketones  $\text{MeCOR}$  with the trimethylsilyl ether of N-trifluoroacetylnorpseudoephedrine in the presence of catalytic amts. of  $\text{Me}_3\text{SiB(OTf)}_4$  or  $\text{Me}_3\text{SiOTf/TfOH}$  ( $\text{Tf} = \text{CF}_3\text{SO}_2$ ) followed by addn. of allyltrimethylsilane. The yield was about 90% (based on conversion) and the diastereoselectivity was about 90:10. Using iso-Pr Me ketone a selectivity of >95:5 was obtained; thus only one diastereomer could be detected.

L4 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1989:553339 CAPLUS

DN 111:153339

TI Preparation of esterified N-(dibenzocycloheptenylideneethyl)ephedrine derivatives with prolonged antiulcer activity

IN Butelman, Federico

PA Etablissement Texcontor, Liechtenstein

SO Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 313885   | A1   | 19890503 | EP 1988-116449  | 19881005 |
|    | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                 |          |
|    |   |      |          | IT 1987-22407   | 19871023 |
|    | US 4935444  | A    | 19900619 | US 1988-254220  | 19881006 |
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|    | JP 01135748   | A2   | 19890529 | JP 1988-264240  | 19881021 |
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|    |   |      |          | US 1988-254220  | 19881006 |

IT 122881-51-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

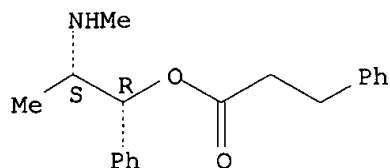
(Reactant or reagent)

(prepn. and N-alkylation of, with (haloethylidene)dibenzocycloheptene)

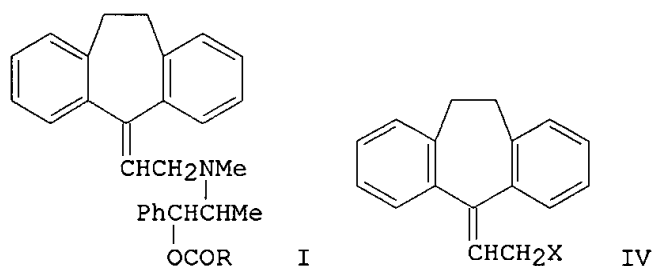
RN 122881-51-0 CAPLUS

CN Benzenepropanoic acid, 2-(methylamino)-1-phenylpropyl ester, [R-(R\*,S\*)]-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB Title compds. [I; R = C<sub>9</sub>H<sub>19</sub>, C<sub>15</sub>H<sub>31</sub>, CH(NH<sub>2</sub>)(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H, (CH<sub>2</sub>)<sub>2</sub>Ph, CMe<sub>3</sub>, p-HOC<sub>6</sub>H<sub>4</sub>, 2-thienyl, 3-pyridyl, 1-amino-2-(5-imidazolyl)ethyl, pamoic acid residue] are prepd. by esterification of ephedrine (II) with RCOCl to give PhCH(O<sub>2</sub>CR)CHMeNHMe (III), followed by N-alkylation with a (haloethylidene)dibenzocycloheptene IV (X = halo). II was esterified by decanoyl chloride (prepd. from the acid) to give 65% III [R = Me(CH<sub>2</sub>)<sub>8</sub>], which was refluxed in MeCN with IV (X = halo, not specified) to give 54% I [R = MeC(CH<sub>2</sub>)<sub>2</sub>]. The latter inhibited stress-induced ulcers in rats with ED<sub>50</sub> of 0.4 and 2.1 mg/kg orally, administered 6 and 36 h prior to commencement of the stress, resp.

L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1979:121187 CAPLUS

DN 90:121187

TI Aminoalcohol derivative

IN Lambelin, Georges; Roncucci, Romeo; Roba, Joseph; Gillet, Claude; Snyers, Michel

PA Continental Pharma, Belg.

SO Ger. Offen., 48 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | DE 2817494 | A1   | 19781109 | DE 1978-2817494 | 19780421 |

|             |    |          |                |          |
|-------------|----|----------|----------------|----------|
| GB 1603379  | A  | 19811125 | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
|             |    |          | GB 1978-27732  | 19780427 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
|             |    |          | GB 1978-16813  | 19780427 |
| GB 1603378  | A  | 19811125 | GB 1978-16813  | 19780427 |
|             |    |          | LU 1977-77237  | 19770503 |
| SE 7804897  | A  | 19781104 | SE 1978-4897   | 19780428 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| NL 7804621  | A  | 19781107 | NL 1978-4621   | 19780428 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| CA 1118438  | A1 | 19820216 | CA 1978-302239 | 19780428 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| US 4474977  | A  | 19841002 | US 1978-901223 | 19780428 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| IL 54608    | A1 | 19840131 | IL 1978-54608  | 19780501 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| FI 7801347  | A  | 19781104 | FI 1978-1347   | 19780502 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| DK 7801898  | A  | 19781104 | DK 1978-1898   | 19780502 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| NO 7801554  | A  | 19781106 | NO 1978-1554   | 19780502 |
| NO 146057   | B  | 19820413 |                |          |
| NO 146057   | C  | 19820721 |                |          |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| ZA 7802507  | A  | 19790725 | ZA 1978-2507   | 19780502 |
|             |    |          | LU 1977-77236  | 19770503 |
| ES 469843   | A1 | 19790916 | ES 1978-469843 | 19780502 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| AT 7803179  | A  | 19800115 | AT 1978-3179   | 19780502 |
| AT 358020   | B  | 19800811 |                |          |
|             |    |          | LU 1977-77236  | 19770503 |
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| FR 2389597  | A1 | 19781201 | FR 1978-13202  | 19780503 |
| FR 2389597  | B1 | 19830819 |                |          |
|             |    |          | LU 1977-77236  | 19770503 |
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| AU 7835733  | A1 | 19791108 | AU 1978-35733  | 19780503 |
| AU 517255   | B2 | 19810716 |                |          |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| CH 635570   | A  | 19830415 | CH 1978-4836   | 19780503 |
|             |    |          | LU 1977-77236  | 19770503 |
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| JP 53141230 | A2 | 19781208 | JP 1978-53627  | 19780504 |
| JP 59040140 | B4 | 19840928 |                |          |
|             |    |          | LU 1977-77236  | 19770503 |

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| AT 7906288 | A | 19810715 | LU 1977-77237 | 19770503 |
| AT 366023  | B | 19820310 | AT 1979-6288  | 19790925 |

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|---------------|----------|
| LU 1977-77236 | 19770503 |
| LU 1977-77237 | 19770503 |
| AT 1978-3179  | 19780502 |

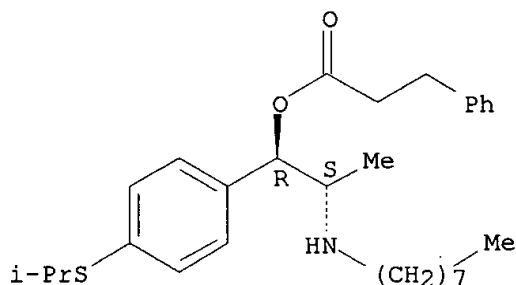
IT 69145-90-0

RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. as muscle relaxant)

RN 69145-90-0 CAPLUS

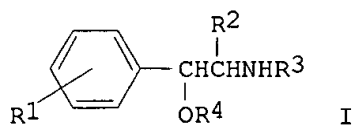
CN Benzenepropanoic acid, 1-[4-[(1-methylethyl)thio]phenyl]-2-  
(octylamino)propyl ester, hydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

GI



AB One hundred three amino alcs. I [R1 = H, C1-5 alkylthio, alkoxy, alkyl, C5-6 cycloalkylthio, cycloalkoxy, cycloalkyl, halo; R2 = C1-3 alkyl; R3 = C1-8 alkyl, C1-4 alkyl, optionally substituted with Ph, PhO, Bz, (un)substituted with alkyl, alkoxy, halo, C6-18 alkenyl, C5-9 cycloalkyl; R4 = COR5 [R5 = C1-10 alkyl, C2-4 alkenyl, C3-8 cycloalkyl, Ph (un)substituted with C1-3 alkyl, alkoxy, halo, C1-4 alkyl, (un)substituted with C1-3 carbalkoxy, alkoxy, NH2, acylamino, C5-6 cycloalkyl, PhO, Ph, optionally substituted with alkyl, alkoxy, halo, cinnamyl], H], useful as antihypertensives, peripheral vasodilators, muscle relaxants, platelet aggregation inhibitors, hypolipemics, and thrombosis inhibitors, were prepd. Thus, acylation of 4-Me2CHSC6H4CH(OH)CHMeNH(CH2)7Me by refluxing with AcCl in C6H6 or PrCOCl gave 70 or 52%, resp. of the corresponding 4-Me2CHSC6H4CH(OR4)CHMeNH(CH2)7Me (R4 = Ac, PrCO).

L4 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2003 ACS  
AN 1973:147610 CAPLUS

DN 78:147610  
 TI Thiamphenicol phenylalaninate  
 IN Saiga, Akisuke; Yamanaka, Motosuke; Sato, Takashi  
 PA Eisai Co., Ltd.  
 SO Jpn. Kokai Tokkyo Koho, 2 pp.  
 CODEN: JKXXAF  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

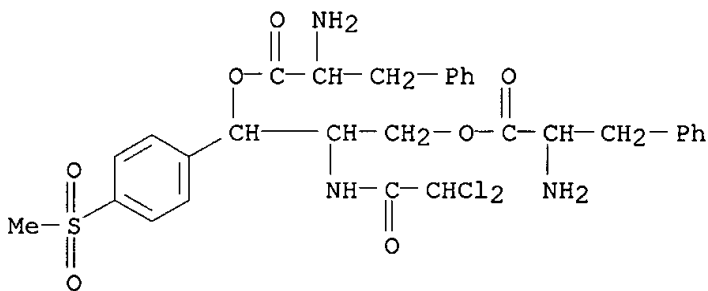
|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|-------------|------|----------|-----------------|----------|
| PI | JP 48004446 | B4   | 19730120 | JP 1971-27212   | 19710427 |

IT **41570-11-0P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

RN 41570-11-0 CAPLUS

CN L-Phenylalanine, 2-[(dichloroacetyl)amino]-1-[4-(methylsulfonyl)phenyl]-1,3-propanediyl ester, [R-(R\*,R\*)]- (9CI) (CA INDEX NAME)



AB A soln. of thiamphenicol and  $\text{PhCH}_2\text{CH}(\text{NH}_2)\text{COCl} \cdot \text{HCl}$  (1:2 by mole) in anhyd. dioxane was stirred 7 hr at 13-17.degree. to give 61.2% thiamphenicol phenylalaninate, which was sol. and stable in  $\text{H}_2\text{O}$ .

L4 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1970:67270 CAPLUS

DN 72:67270

TI Water soluble antibiotic chloramphenicol .beta.-phenylalanine ester salts

IN Zumin, Silva T.; Mosna, Sergio

PA Pierrel S.p.A.

SO Brit., 8 pp.

CODEN: BRXXAA

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | GB 1173562 |      | 19691210 | GB              | 19660425 |

IT **25613-59-6P 25613-62-1P 25613-63-2P**

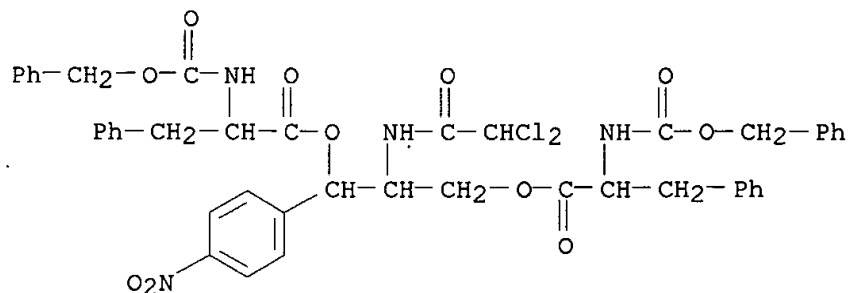
**25613-64-3P 25616-21-1P 25616-22-2P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

RN 25613-59-6 CAPLUS

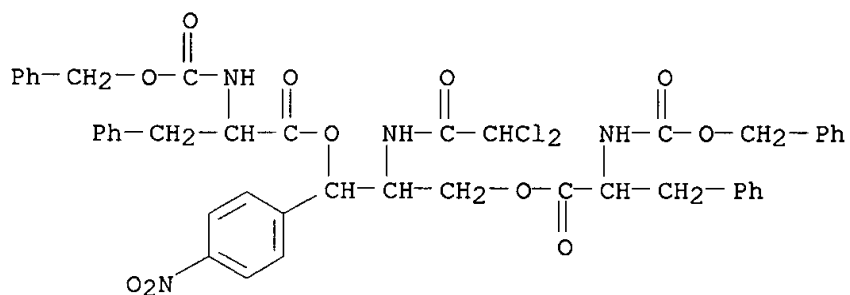
CN Alanine, N-carboxy-3-phenyl-, N-benzyl ester, L-, diester with  
 D-threo-2,2-dichloro-N-[(.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-

nitrophenethyl]acetamide (8CI) (CA INDEX NAME)



RN 25613-62-1 CAPLUS

CN Alanine, N-carboxy-3-phenyl-, N-benzyl ester, DL-, diester with  
D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-  
nitrophenethyl]acetamide (8CI) (CA INDEX NAME)



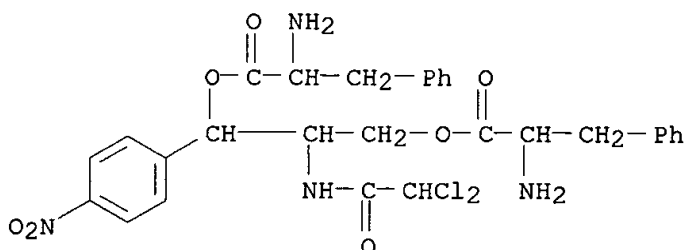
RN 25613-63-2 CAPLUS

CN Alanine, phenyl-, L-, diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-  
.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide, bis(trifluoroacetate)  
(8CI) (CA INDEX NAME)

CM 1

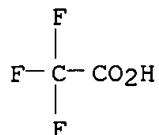
CRN 47832-98-4

CMF C29 H30 Cl2 N4 O7

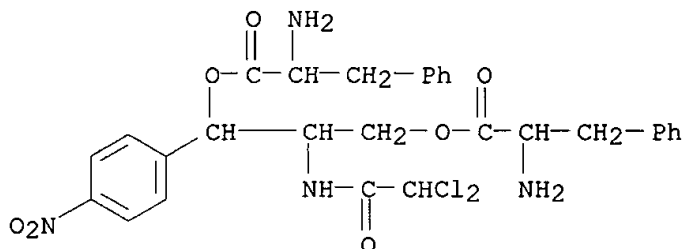


CM 2

CRN 76-05-1  
CMF C2 H F3 O2



RN 25613-64-3 CAPLUS  
CN Alanine, phenyl-, L-, diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide, dihydrochloride (8CI)  
(CA INDEX NAME)

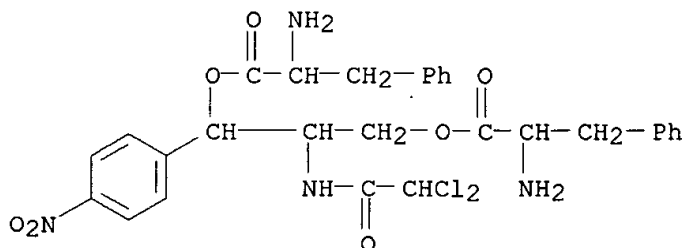


● 2 HCl

RN 25616-21-1 CAPLUS  
CN Alanine, N-acetyl-3-phenyl-, L-, compd. with L-phenylalanine diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide (2:1) (8CI) (CA INDEX NAME)

CM 1

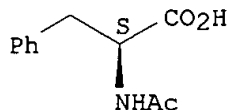
CRN 47832-98-4  
CMF C29 H30 Cl2 N4 O7



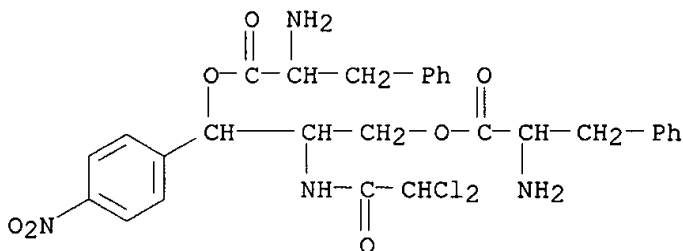
CM 2

CRN 2018-61-3  
CMF C11 H13 N O3

Absolute stereochemistry. Rotation (+).



RN 25616-22-2 CAPLUS  
CN Alanine, phenyl-, DL-, diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide, dihydrobromide (8CI)  
(CA INDEX NAME)



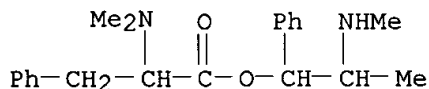
●2 HBr

AB Salts of chloramphenicol 1,3-bis(L-.beta.-phenylalaninate) (I) and chloramphenicol 3-L-.beta.-phenylalaninate (II), useful for parenteral administration, with antibiotic activity, were prepd. by reacting D-(-)-threo-1-p-nitrophenyl-2-dichloroacetamido-1,3-propanediol (chloramphenicol) (III) either with N-carbobenzoxy-L-.beta.-phenylalanine (IV) in the presence of dicyclo-hexylcarbodiimide (V) and anhyd. pyridine (VI) or with IV anhydride (VII) in the presence of VI to give chloramphenicol 1,3-bis(N-carbobenzoxy-L-.beta.-phenylalaninate) (VIII) and chloramphenicol 3-(N-carbobenzoxy-L-.beta.-phenylalaninate) (IX), resp., followed by removal of the protecting group(s) by treatment with aq. HBr or anhyd. CF<sub>3</sub>CO<sub>2</sub>H. I and II are hydrolyzed in vivo to III and phenylalanine. Thus, addn. of 10.30 g V at 15.degree. to a stirred soln. of 29.93 g IV in 150 ml Me<sub>2</sub>CO, and the mixt. stirred 3 hr gave 96.5% VII. Racemic N-carbobenzoxy-DL-.beta.-phenylalanine anhydride (X) (93.5%) was prepd. similarly. III (5.82 g) in 10 ml VI was added to 180 ml of an Me<sub>2</sub>CO soln. of 25.2 g VII and the mixt. stirred 5-6 hr at room temp. and poured on ice-HCl to give, after treatment with 3.5 ml p-H<sub>2</sub>N-C<sub>6</sub>H<sub>4</sub>-NMe<sub>2</sub> (XI) in dry C<sub>6</sub>H<sub>6</sub> to remove excess VII, 90% VIII, m. 95-7.degree.. Racemic chloramphenicol 1,3-bis(N-carbobenzoxy-.beta.-phenylalaninate) (XII) (94%), a yellow oil, was prepd. similarly from X. IV (22.45 g) and 15 ml VI added to a stirred soln. of 9.69 g III in 60 ml HCONMe<sub>2</sub>, the soln. cooled to -5 to -8.degree., 18.57 g V added slowly, the mixt. stirred 1 hr, kept 3 hr at -5.degree. and poured on a mixt. of 50 ml concd. HCl, 50 ml H<sub>2</sub>O, and 100 g ice gave a ppt., which was centrifuged off and extd.



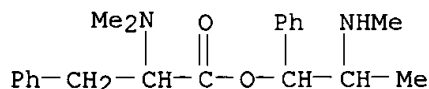
with C<sub>6</sub>H<sub>6</sub>. Treatment of the C<sub>6</sub>H<sub>6</sub> ext. with 3.5 ml XI gave 93% VIII, m. 95-7.degree.. IX, m. 145-7.degree., was prepd. similarly using 19.39 g III, 60 ml HCONMe<sub>2</sub>, 17.96 g IV, 15 ml VI, and 12.38 g V. A mixt. of 17.72 g VIII and 40 ml anhyd. CF<sub>3</sub>CO<sub>2</sub>H refluxed 1 hr in the presence of 8 g resorcinol gave 16.30 g I.CF<sub>3</sub>CO<sub>2</sub>H (XIII). Addn. of XIII to satd. aq. NaHCO<sub>3</sub>, extn. of the free base with CH<sub>2</sub>Cl<sub>2</sub>, and treatment of the ext. with HCl gave I.HCl, m. 220-222.degree. (decompn.). II.HCl, [.alpha.]<sub>D</sub><sup>20</sup> 10.77.degree. (c 2, H<sub>2</sub>O), was prepd. similarly from IX. A soln. of 5 g XII in 60 ml 2.5N HBr in AcOH stirred 10 min at 25 .degree. gave 85% a mixt. of chloramphenicol 1,3-bis(D- and L-.beta.-phenylalaninate-HBr) sepd. by chromatog. XIII (13 g) treated with satd. aq. NaHCO<sub>3</sub>, extn. of the free base with CH<sub>2</sub>Cl<sub>2</sub>, and treatment of the ext. with N-acetyl-L-phenylalanine gave III 1,3-bis(L-.beta.-phenylalaninate N-acetyl-L-phenylalaninate); III 3-(L-.beta.-phenylalaninate N-acetyl-L-phenylalaninate) was prepd. similarly.

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2003 ACS  
 AN 1967:402830 CAPLUS  
 DN 67:2830  
 TI Separation of the organic bases by Craig partition. VII. Acyl migration in the stereoisomeric N-(N,N-dimethylphenylalanyl)ephedrines  
 AU Schoenenberger, Helmut; Fuchsberger, K. D.; Brinkmann, Rolf  
 CS Univ. Munich, Munich, Fed. Rep. Ger.  
 SO Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft (1967), 300(2), 126-35  
 CODEN: APBDAJ; ISSN: 0376-0367  
 DT Journal  
 LA German  
 IT **14355-01-2P 14355-02-3P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 14355-01-2 CAPLUS  
 CN Alanine, N,N-dimethyl-3-phenyl-, ester with (-)-pseudoephedrine, dihydrochloride, L- (8CI) (CA INDEX NAME)

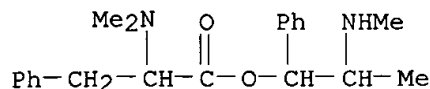


● 2 HCl

RN 14355-02-3 CAPLUS  
 CN Alanine, N,N-dimethyl-3-phenyl-, ester with (-)-pseudoephedrine, dihydrochloride, D- (8CI) (CA INDEX NAME)



2 HCl



● 2 HCl

AB cf. CA 66: 49281u. The compds. studied were N-(L-N,N-dimethylphenylalanyl)-L-ephedrine (I), N-(D-N,N-dimethylphenylalanyl)-L-ephedrine (II), N-(L-N,N-dimethylphenylalanyl)-L-pseudoephedrine (III), and N-(D-N,N-dimethylphenylalanyl)-L-pseudoephedrine (IV). In every case, only the ester of L-pseudoephedrine resulted, even under mild conditions (room temp., acetone-HCl). Complete inversion of the erythro derivs. occurred. In 2N HCl at 80.degree., the ester from I formed quant. in 10 min. while that from III (retention of configuration) required 25 hrs. With II, 5 hrs. and with IV, 22 hrs. were required. The 4 amides pass through either of 2 cyclic intermediates during the migration, L,L-(V) or D,L-pseudooxazolidine (VI). The rates are explained by steric considerations of the mechanism, V resulting from I via inversion and from III with retention, and VI, from II via inversion and IV with retention. Craig partition as described previously (loc. cit.) was used to sep. and det. the reaction products. Twenty-four partition steps using a solvent mixt. of 0.5M citrate buffer (pH 4/5)-MeOH-CHCl<sub>3</sub> (9:1:10 parts by vol.) were required for sepn. into N- and O-aminoacylphenedrines. The O-(L-N,N-dimethylphenylalanyl)-L-pseudoephedrine m. 170-2.degree., [.alpha.]<sub>D</sub><sup>20</sup> + 114.degree. (c = 0.0055 g./ml., 5N HCl) and the O-(D-N,N-dimethyl-) ester melts at 174-6.degree., [.alpha.]<sub>D</sub><sup>20</sup> 48.degree. (c 0.0055 g./ml., 5N HCl).

=> d cost

|  |                  |               |
|--|------------------|---------------|
| COST IN U.S. DOLLARS                       | SINCE FILE ENTRY | TOTAL SESSION |
| CONNECT CHARGES                            | 0.34             | 0.83          |
| NETWORK CHARGES                            | 0.06             | 0.18          |
| SEARCH CHARGES                             | 0.00             | 147.75        |
| DISPLAY CHARGES                            | 43.20            | 43.20         |
|  | -----            | -----         |
|  | 43.60            | 191.96        |
| CAPLUS FEE (5%)                            | 2.18             | 2.18          |
|  | -----            | -----         |
| FULL ESTIMATED COST                        | 45.78            | 194.14        |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE                        | -6.51            | -6.51         |

IN FILE 'CAPLUS' AT 14:38:52 ON 26 MAY 2003

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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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|------|----|--------|---|
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| NEWS | 2  | Apr 08 | "Ask CAS" for self-help around the clock  |
| NEWS | 3  | Jun 03 | New e-mail delivery for search results now available  |
| NEWS | 4  | Aug 08 | PHARMAMarketLetter(PHARMAML) - new on STN   |
| NEWS | 5  | Aug 19 | Aquatic Toxicity Information Retrieval (AQUIRE)<br>now available on STN                       |
| NEWS | 6  | Aug 26 | Sequence searching in REGISTRY enhanced   |
| NEWS | 7  | Sep 03 | JAPIO has been reloaded and enhanced  |
| NEWS | 8  | Sep 16 | Experimental properties added to the REGISTRY file  |
| NEWS | 9  | Sep 16 | CA Section Thesaurus available in CAPLUS and CA   |
| NEWS | 10 | Oct 01 | CASREACT Enriched with Reactions from 1907 to 1985  |
| NEWS | 11 | Oct 24 | BEILSTEIN adds new search fields  |
| NEWS | 12 | Oct 24 | Nutraceuticals International (NUTRACEUT) now available on STN                                 |
| NEWS | 13 | Nov 18 | DKILIT has been renamed APOLLIT   |
| NEWS | 14 | Nov 25 | More calculated properties added to REGISTRY  |
| NEWS | 15 | Dec 04 | CSA files on STN  |
| NEWS | 16 | Dec 17 | PCTFULL now covers WP/PCT Applications from 1978 to date                                      |
| NEWS | 17 | Dec 17 | TOXCENTER enhanced with additional content  |
| NEWS | 18 | Dec 17 | Adis Clinical Trials Insight now available on STN   |
| NEWS | 19 | Jan 29 | Simultaneous left and right truncation added to COMPENDEX,<br>ENERGY, INSPEC                  |
| NEWS | 20 | Feb 13 | CANCERLIT is no longer being updated  |
| NEWS | 21 | Feb 24 | METADEx enhancements  |
| NEWS | 22 | Feb 24 | PCTGEN now available on STN   |
| NEWS | 23 | Feb 24 | TEMA now available on STN   |
| NEWS | 24 | Feb 26 | NTIS now allows simultaneous left and right truncation  |
| NEWS | 25 | Feb 26 | PCTFULL now contains images   |
| NEWS | 26 | Mar 04 | SDI PACKAGE for monthly delivery of multifile SDI results                                     |
| NEWS | 27 | Mar 20 | EVENTLINE will be removed from STN  |
| NEWS | 28 | Mar 24 | PATDPAFULL now available on STN   |
| NEWS | 29 | Mar 24 | Additional information for trade-named substances without<br>structures available in REGISTRY |
| NEWS | 30 | Apr 11 | Display formats in DGENE enhanced   |
| NEWS | 31 | Apr 14 | MEDLINE Reload  |
| NEWS | 32 | Apr 17 | Polymer searching in REGISTRY enhanced  |
| NEWS | 33 | Apr 21 | Indexing from 1947 to 1956 being added to records in CA/CAPLUS                                |
| NEWS | 34 | Apr 21 | New current-awareness alert (SDI) frequency in<br>WPIDS/WPINDEX/WPIX                          |
| NEWS | 35 | Apr 28 | RDISCLOSURE now available on STN  |
| NEWS | 36 | May 05 | Pharmacokinetic information and systematic chemical names<br>added to PHAR                    |
| NEWS | 37 | May 15 | MEDLINE file segment of TOXCENTER reloaded  |
| NEWS | 38 | May 15 | Supporter information for ENCOMPPAT and ENCOMPLIT updated                                     |
| NEWS | 39 | May 16 | CHEMREACT will be removed from STN  |

NEWS 40 May 19 Simultaneous left and right truncation added to WSCA  
NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and  
right truncation

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT  
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),  
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003  
NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS INTER General Internet Information  
NEWS LOGIN Welcome Banner and News Items  
NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that  
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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 14:37:32 ON 26 MAY 2003

=> file reg

| COST IN U.S. DOLLARS | SINCE FILE<br>ENTRY | TOTAL<br>SESSION |
|----------------------|---------------------|------------------|
| FULL ESTIMATED COST  | 0.21                | 0.21             |

FILE 'REGISTRY' ENTERED AT 14:37:43 ON 26 MAY 2003

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STRUCTURE FILE UPDATES: 25 MAY 2003 HIGHEST RN 519753-05-0

DICTIONARY FILE UPDATES: 25 MAY 2003 HIGHEST RN 519753-05-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNote 27, Searching Properties  
in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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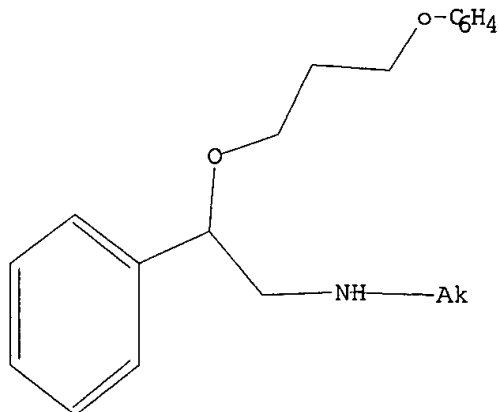
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L1 STRUCTURE UPLOADED

=&gt; d l1

L1 HAS NO ANSWERS

L1 STR



G1 NH,X,Hy

Structure attributes must be viewed using STN Express query preparation.

=&gt; s l1

SAMPLE SEARCH INITIATED 14:38:06 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1045 TO ITERATE

95.7% PROCESSED 1000 ITERATIONS  
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)  
SEARCH TIME: 00.00.01

1 ANSWERS

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 18961 TO 22839  
PROJECTED ANSWERS: 1 TO 81

L2 1 SEA SSS SAM L1

=&gt; s l1 sss full

FULL SEARCH INITIATED 14:38:13 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 20951 TO ITERATE

100.0% PROCESSED 20951 ITERATIONS  
SEARCH TIME: 00.00.01

24 ANSWERS

L3 24 SEA SSS FUL L1

=&gt; file caplus

COST IN U.S. DOLLARS

SINCE FILE  
ENTRY

TOTAL  
SESSION

FULL ESTIMATED COST

148.15

148.36

FILE 'CAPLUS' ENTERED AT 14:38:21 ON 26 MAY 2003

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FILE COVERS 1907 - 26 May 2003 VOL 138 ISS 22  
FILE LAST UPDATED: 25 May 2003 (20030525/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

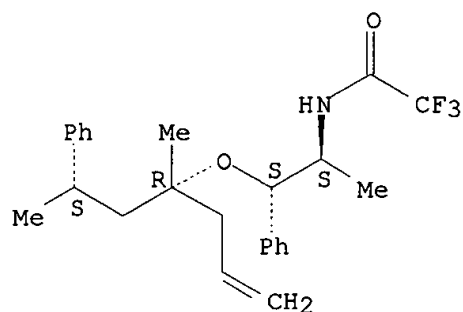
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L4 10 L3

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L4 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2003 ACS  
AN 2001:57805 CAPLUS  
DN 134:252075  
TI Synthesis of enantiopure homoallylic ethers by reagent controlled facial selective allylation of chiral ketones  
AU Tietze, Lutz F.; Weigand, Berthold; Volkel, Ludwig; Wulff, Christian; Bittner, Christian  
CS Institut fur Organische Chemie Georg-August-Universitat Gottingen, Gottingen, 37077, Germany  
SO Chemistry--A European Journal (2001), 7(1), 161-168  
CODEN: CEUJED; ISSN: 0947-6539  
PB Wiley-VCH Verlag GmbH  
DT Journal  
LA English  
OS CASREACT 134:252075  
IT **330798-68-0P 330798-69-1P**  
RL: BYP (Byproduct); SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of enantiopure homoallylic ethers by reagent controlled facial selective allylation of chiral ketones)  
RN 330798-68-0 CAPLUS  
CN Acetamide, 2,2,2-trifluoro-N-[(1S,2S)-1-methyl-2-[[ (1R)-1-methyl-1-{ (2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

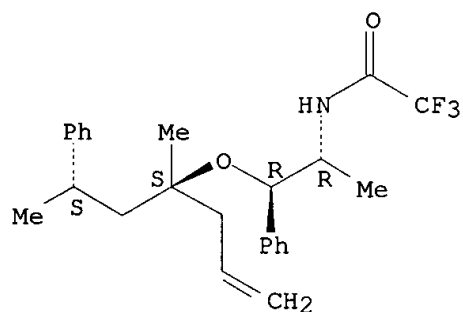
Absolute stereochemistry.



RN 330798-69-1 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[[(1S)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

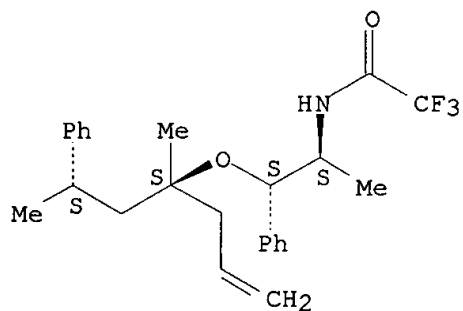
Absolute stereochemistry.

IT 330798-62-4P 330798-63-5P 330798-73-7P  
330798-76-0PRL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of enantiopure homoallylic ethers by reagent controlled  
facial selective allylation of chiral ketones)

RN 330798-62-4 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1S,2S)-1-methyl-2-[[[(1S)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

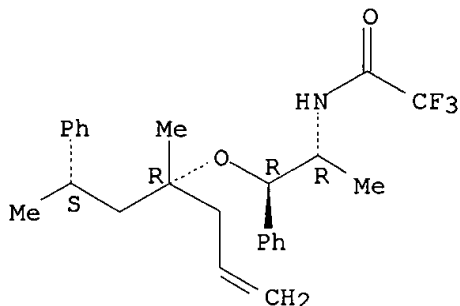
Absolute stereochemistry. Rotation (-).



RN 330798-63-5 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1R)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

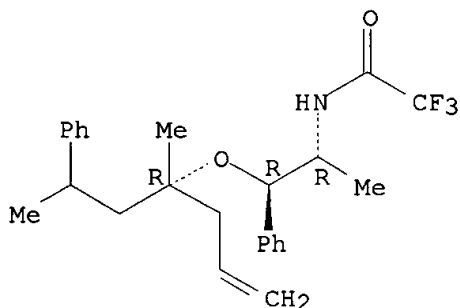
Absolute stereochemistry. Rotation (+).



RN 330798-73-7 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1R)-1-methyl-1-(2-phenylpropyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

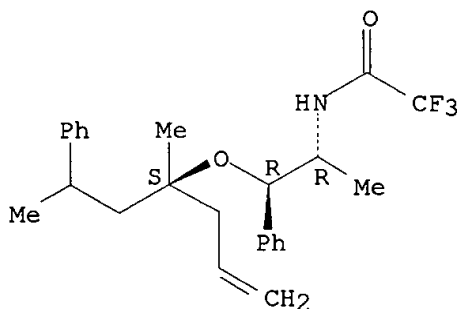
Absolute stereochemistry.



RN 330798-76-0 CAPLUS

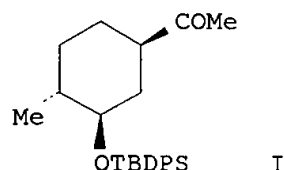
CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1S)-1-methyl-1-(2-phenylpropyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI





AB The stereoselective allylation of chiral Me ketones to give tertiary homoallylic ethers, which can easily be transformed into homoallylic alcs., is described. Reaction of the enantiopure ketones (I), (R)-Me<sub>2</sub>CH(CH<sub>2</sub>)<sub>3</sub>CH(.beta.Me)CH<sub>2</sub>COMe, (R)-MeCH(.beta.OSiPh<sub>2</sub>CMe<sub>3</sub>)CH<sub>2</sub>COMe, (S)-MeCH(.alpha.Ph)CH<sub>2</sub>COMe and the racemic ketones MeCH(OSiPh<sub>2</sub>CMe<sub>3</sub>)CH<sub>2</sub>COMe, MeCH(Ph)CH<sub>2</sub>COMe, MeCH<sub>2</sub>CH(Ph)COMe, MeCH<sub>2</sub>CH(Me)COMe with the norpseudoephedrine deriv. and allylsilane in the presence of a catalytic amt. of trifluoromethanesulfonic acid, led to a series of homoallylic ethers with good to excellent diastereoselectivity (85:15 to > 97:3). The allylation is reagent controlled and nearly independent from the stereogenic centers in the substrates. A partial kinetic resolu. was obsd. using the racemic ketones. In the reaction of the chiral ketones with the achiral reagents ethoxytrimethylsilane and allylsilane only a low diastereoselectivity was obsd.

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1998:625620 CAPLUS

DN 129:316000

TI Synthesis of enantiopure homoallylic alcohols by a highly selective asymmetric allylation of ketones

AU Tietze, Lutz F.; Schiemann, Kai; Wegner, Christoph; Wulff, Christian

CS Institute Organic Chemistry, Georg-August-Universitat Gottingen, Gottingen, D-37077, Germany

SO Chemistry--A European Journal (1998), 4(9), 1862-1869

CODEN: CEUJED; ISSN: 0947-6539

PB Wiley-VCH Verlag GmbH

DT Journal

LA English

OS CASREACT 129:316000

IT 165823-95-0P

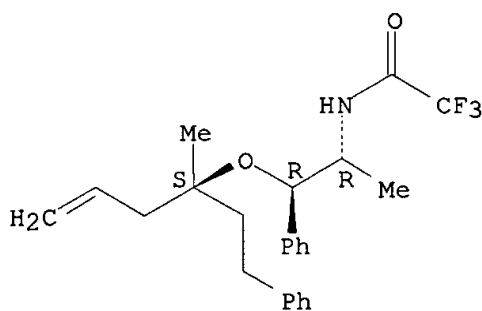
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of enantiopure homoallylic alcs. by asym. allylation of ketones)

RN 165823-95-0 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1S)-1-methyl-1-(2-phenylethyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB A highly selective asym. domino allylation of aliph. ketones is described. When Me ketones, (R,R)-Me<sub>2</sub>SiOCHPhCHMeNHCOCF<sub>3</sub>, and CH<sub>2</sub>:CHCH<sub>2</sub>SiMe<sub>3</sub> react in the presence of catalytic amts. of trifluoromethanesulfonic acid, the homoallylic ethers are produced with up to 24:1 diastereoselectivity and 89% yield. Ether cleavage using lithium or sodium in liq. ammonia gives the homoallylic alcs. in 75 to 95% yield and up to 92% ee. Even EtCOMe, the most difficult example, showed a stereoselectivity of 9:1 at -78.degree.C and 24:1 at -109.degree.C. In addn., the allylation of protected hydroxyalkyl Me ketones gave the corresponding homoallylic ethers with a diastereoselectivity of up to >244:1 and 98% yield. In contrast, Et alkyl ketones have a low selectivity.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1997:639948 CAPLUS

DN 127:307269

TI Preparation of optically active succinic acid derivatives. I. Optical resolution of 2-benzyl-3-(cis-hexahydroisoindolin-2-ylcarbonyl)propionic acid

AU Yamaguchi, Toshiaki; Yanagi, Takashi; Hokari, Hiroshi; Mukaiyama, Yuko; Kamijo, Tetsuhide; Yamamoto, Iwao

CS Kissei Pharmaceutical Co., Ltd., Central Research Laboratories, Hotaka, 399-83, Japan

SO Chemical & Pharmaceutical Bulletin (1997), 45(9), 1518-1520

CODEN: CPBTAL; ISSN: 0009-2363

PB Pharmaceutical Society of Japan

DT Journal

LA English

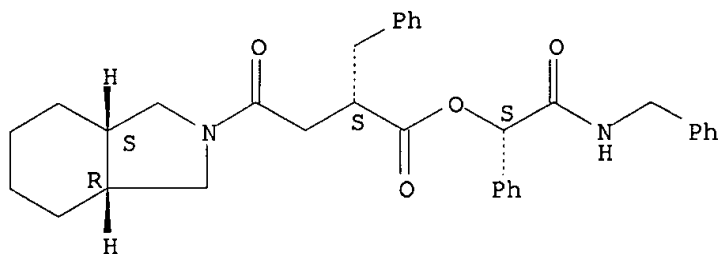
IT 197447-44-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(optical resolu. of benzyl(hexahydroisoindolinylcarbonyl)propionic acid)

RN 197447-44-2 CAPLUS

CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, 2-oxo-1-phenyl-2-[(phenylmethyl)amino]ethyl ester, [2(.alpha.S)-[2[R\*(R\*)],3a.alpha.,7a.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



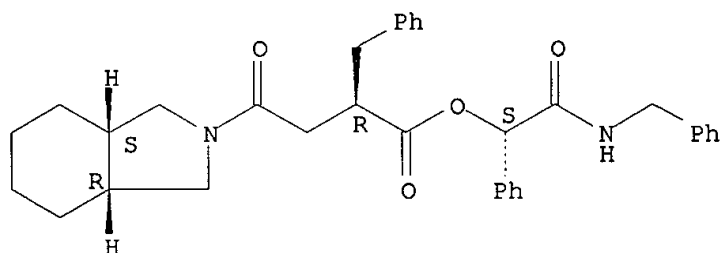
IT 197447-45-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(optical resolu. of benzyl(hexahydroisoindolinylcarbonyl)propionic acid)

RN 197447-45-3 CAPLUS

CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-  
, 2-oxo-1-phenyl-2-[(phenylmethyl)amino]ethyl ester, [2(.alpha.R)-  
[2[R\*(S\*)],3a.alpha.,7a.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB Optical resolu. of 2-benzyl-3-(cis-hexahydroisoindolin-2-ylcarbonyl)propionic acid (I) was accomplished by two methods. Thus, I was esterified with (S)-N-benzylmandelamide and the resulting diastereomeric esters were sepd. by column chromatog. on silica gel. One of the diastereomers was hydrolyzed to give the optically active acid (-)-I. The abs. configuration of (-)-I was established as S by comparison with an authentic sample. The alternative method was resolu. using an optically active amine. Treatment of a soln. of the racemic acid I with 0.65 equiv of (R)-1-(1-naphthyl)ethylamine in ethanol gave the salt in 23.2% yield with an optical purity of 96.8% ee.

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1995:835557 CAPLUS

DN 123:256542

TI Preparation of annelated dihydropyridines

IN Roos, Otto; Loesel, Walter; Arndts, Dietrich

PA Boehringer Ingelheim KG, Germany

SO Ger. Offen., 28 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

PATENT NO.

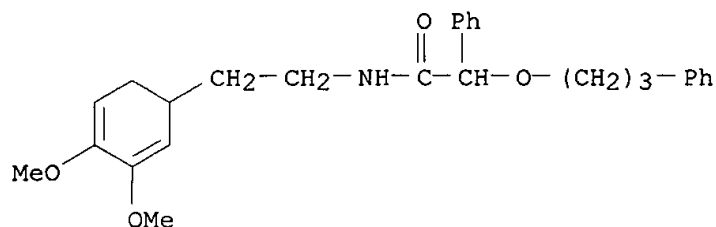
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DATE

APPLICATION NO.

DATE

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|    | CA 2178209   | AA | 19950629 | CA 1994-2178209           | 19941214 |
|    |  |    |          | DE 1993-4343683A          | 19931221 |
| WO | 9517389  | A1 | 19950629 | WO 1994-EP4150            | 19941214 |
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|    |  |    |          | DE 1993-4343683A          | 19931221 |
| AU | 9512433  | A1 | 19950710 | AU 1995-12433             | 19941214 |
| AU | 699208   | B2 | 19981126 |                           |          |
|    |  |    |          | DE 1993-4343683A          | 19931221 |
|    |  |    |          | WO 1994-EP4150 W          | 19941214 |
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|    |  |    |          | DE 1993-4343683A          | 19931221 |
|    |  |    |          | WO 1994-EP4150 W          | 19941214 |
| CN | 1138325  | A  | 19961218 | CN 1994-194572            | 19941214 |
| CN | 1044905  | B  | 19990901 |                           |          |
|    |  |    |          | DE 1993-4343683A          | 19931221 |
| JP | 09506882   | T2 | 19970708 | JP 1994-517154            | 19941214 |
|    |  |    |          | DE 1993-4343683A          | 19931221 |
|    |  |    |          | WO 1994-EP4150 W          | 19941214 |
| RU | 2136664  | C1 | 19990910 | RU 1996-115153            | 19941214 |
|    |  |    |          | DE 1993-4343683A          | 19931221 |
|    |  |    |          | WO 1994-EP4150 W          | 19941214 |
| AT | 194978   | E  | 20000815 | AT 1995-903342            | 19941214 |
|    |  |    |          | DE 1993-4343683A          | 19931221 |
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| ES | 2149958  | T3 | 20001116 | ES 1995-903342            | 19941214 |
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|    |  |    |          | DE 1993-4343683A          | 19931221 |
| US | 5661157  | A  | 19970826 | US 1994-360867            | 19941221 |
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| TW | 404941   | B  | 20000911 | TW 1994-83112295          | 19941228 |
|    |  |    |          | DE 1993-4343683A          | 19931221 |
| US | 5968948  | A  | 19991019 | US 1997-857643            | 19970516 |
|    |  |    |          | DE 1993-4343683A          | 19931221 |
|    |  |    |          | US 1994-360867 A319941221 |          |
| US | 6136819  | A  | 20001024 | US 1999-329443            | 19990610 |
|    |  |    |          | DE 1993-4343683A          | 19931221 |
|    |  |    |          | US 1994-360867 A319941221 |          |
|    |  |    |          | US 1997-857643 A319970516 |          |
| OS | MARPAT 123:256542  |    |          |                           |          |
| IT | <b>168545-16-2P</b>  |    |          |                           |          |
|    | RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)                      |    |          |                           |          |
|    | (prepn. of annelated dihydropyridines from)  |    |          |                           |          |
| RN | 168545-16-2 CAPLUS   |    |          |                           |          |
| CN | Benzeneacetamide, N-[2-(3,4-dimethoxy-2,4-cyclohexadien-1-yl)ethyl]-.alpha.-(3-phenylpropoxy)- (9CI) (CA INDEX NAME) |    |          |                           |          |



GI For diagram(s), see printed CA Issue.

AB The title compds. [I; A = benzo, thieno, indolo; B = O, S, (un)substituted CH<sub>2</sub>; R<sub>2</sub> = OH, alkoxy, benzyloxy, halogen, alkyl, methanesulfonyloxy, etc.; R<sub>3</sub> = 2- or 3-thienyl, (un)substituted Ph, alkyl, cycloalkylalkyl; R<sub>4</sub> = (un)branched alkenyl or alkynyl, alkoxy, dialkylamino, heterocyclyl, Ph, etc.; m = 0-3] (e.g., II), useful as calcium-channel blockers (no data), are prepd. by the intramol. cyclocondensation of arom. amides (III) (e.g., IV) in the presence of condensing agents (e.g., POCl<sub>3</sub>), and I-contg. formulations are also presented.

L4 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1995:568922 CAPLUS

DN 123:111518

TI Enantioselective Synthesis of Tertiary Homoallylic Alcohols via Diastereoselective Addition of Allylsilanes to Ketones

AU Tietze, Lutz F.; Schiemann, Kai; Wegner, Christoph

CS Institute of Organic Chemistry, Georg-August-Universitaet, Goettingen, D-37077, Germany

SO Journal of the American Chemical Society (1995), 117(21), 5851-2

CODEN: JACSAT; ISSN: 0002-7863

PB American Chemical Society

DT Journal

LA English

OS CASREACT 123:111518

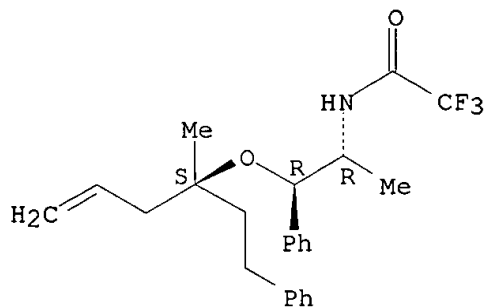
IT 165823-95-0P 166021-67-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(enantioselective synthesis of tertiary homoallylic alcs. via diastereoselective addn. of allylsilanes to ketones)

RN 165823-95-0 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1S)-1-methyl-1-(2-phenylethyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

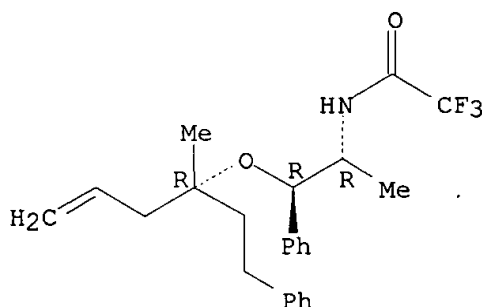
Absolute stereochemistry. Rotation (+).



RN 166021-67-6 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[1-methyl-2-[[1-methyl-1-(2-phenylethyl)-3-butenyl]oxy]-2-phenylethyl]-, [1R-[1R\*,2R\*(R\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Enantiopure tertiary homoallylic alcs.  $\text{CH}_2\text{:CHCH}_2\text{CRMeOH}$  ( $\text{R} = \text{alkyl}$ ) can be obtained from the corresponding homoallylic ethers  $\text{CH}_2\text{:CHCH}_2\text{CRMeOR}_1$  [4,  $\text{R}_1 = \text{residue of (1R,2R)-N-(trifluoroacetyl)norpseudoephedrine}$ ] by treatment with sodium in liq. ammonia. The ethers 4 are formed highly selectively by treatment of the ketones  $\text{MeCOR}$  with the trimethylsilyl ether of N-trifluoroacetylnorpseudoephedrine in the presence of catalytic amts. of  $\text{Me}_3\text{SiB(OTf)}_4$  or  $\text{Me}_3\text{SiOTf/TfOH}$  ( $\text{Tf} = \text{CF}_3\text{SO}_2$ ) followed by addn. of allyltrimethylsilane. The yield was about 90% (based on conversion) and the diastereoselectivity was about 90:10. Using iso-Pr Me ketone a selectivity of >95:5 was obtained; thus only one diastereomer could be detected.

L4 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1989:553339 CAPLUS

DN 111:153339

TI Preparation of esterified N-(dibenzocycloheptenylideneethyl)ephedrine derivatives with prolonged antiulcer activity

IN Butelman, Federico

PA Etablissement Texcontor, Liechtenstein

SO Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 313885   | A1   | 19890503 | EP 1988-116449  | 19881005 |
|    | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                 |          |
|    | US 4935444  | A    | 19900619 | IT 1987-22407   | 19871023 |
|    |   |      |          | US 1988-254220  | 19881006 |
|    |   |      |          | IT 1987-22407   | 19871023 |
|    | JP 01135748   | A2   | 19890529 | JP 1988-264240  | 19881021 |
|    |   |      |          | IT 1987-22407   | 19871023 |
|    | US 4990522  | A    | 19910205 | US 1990-487277  | 19900302 |
|    |   |      |          | IT 1987-22407   | 19871023 |
|    |   |      |          | US 1988-254220  | 19881006 |

IT 122881-51-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

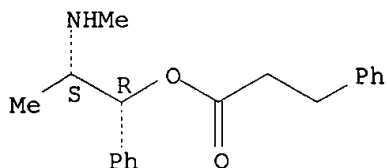
(Reactant or reagent)

(prepn. and N-alkylation of, with (haloethylidene)dibenzocycloheptene)

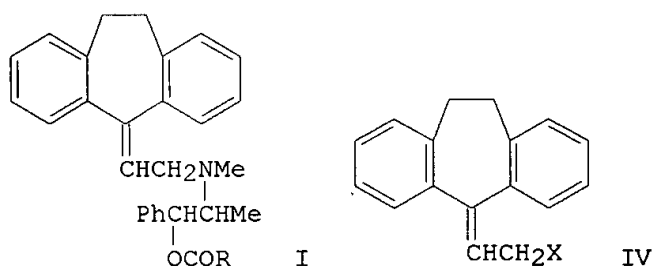
RN 122881-51-0 CAPLUS

CN Benzenepropanoic acid, 2-(methylamino)-1-phenylpropyl ester, [R-(R\*,S\*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB Title compds. [I; R = C<sub>9</sub>H<sub>19</sub>, C<sub>15</sub>H<sub>31</sub>, CH(NH<sub>2</sub>)(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H, (CH<sub>2</sub>)<sub>2</sub>Ph, CMe<sub>3</sub>, p-HOC<sub>6</sub>H<sub>4</sub>, 2-thienyl, 3-pyridyl, 1-amino-2-(5-imidazolyl)ethyl, pamoic acid residue] are prepd. by esterification of ephedrine (II) with RCOCl to give PhCH(O<sub>2</sub>CR)CHMeNHMe (III), followed by N-alkylation with a (haloethylidene)dibenzocycloheptene IV (X = halo). II was esterified by decanoyl chloride (prepd. from the acid) to give 65% III [R = Me(CH<sub>2</sub>)<sub>8</sub>], which was refluxed in MeCN with IV (X = halo, not specified) to give 54% I [R = MeC(CH<sub>2</sub>)<sub>2</sub>]. The latter inhibited stress-induced ulcers in rats with ED<sub>50</sub> of 0.4 and 2.1 mg/kg orally, administered 6 and 36 h prior to commencement of the stress, resp.

L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1979:121187 CAPLUS

DN 90:121187

TI Aminoalcohol derivative

IN Lambelin, Georges; Roncucci, Romeo; Roba, Joseph; Gillet, Claude; Snyers, Michel

PA Continental Pharma, Belg.

SO Ger. Offen., 48 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | DE 2817494 | A1   | 19781109 | DE 1978-2817494 | 19780421 |

|             |    |          |                |          |
|-------------|----|----------|----------------|----------|
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| GB 1603379  | A  | 19811125 | GB 1978-27732  | 19780427 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
|             |    |          | GB 1978-16813  | 19780427 |
| GB 1603378  | A  | 19811125 | GB 1978-16813  | 19780427 |
|             |    |          | LU 1977-77237  | 19770503 |
| SE 7804897  | A  | 19781104 | SE 1978-4897   | 19780428 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| NL 7804621  | A  | 19781107 | NL 1978-4621   | 19780428 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| CA 1118438  | A1 | 19820216 | CA 1978-302239 | 19780428 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| US 4474977  | A  | 19841002 | US 1978-901223 | 19780428 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| IL 54608    | A1 | 19840131 | IL 1978-54608  | 19780501 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| FI 7801347  | A  | 19781104 | FI 1978-1347   | 19780502 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| DK 7801898  | A  | 19781104 | DK 1978-1898   | 19780502 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| NO 7801554  | A  | 19781106 | NO 1978-1554   | 19780502 |
| NO 146057   | B  | 19820413 |                |          |
| NO 146057   | C  | 19820721 |                |          |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| ZA 7802507  | A  | 19790725 | ZA 1978-2507   | 19780502 |
|             |    |          | LU 1977-77236  | 19770503 |
| ES 469843   | A1 | 19790916 | ES 1978-469843 | 19780502 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| AT 7803179  | A  | 19800115 | AT 1978-3179   | 19780502 |
| AT 358020   | B  | 19800811 |                |          |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| FR 2389597  | A1 | 19781201 | FR 1978-13202  | 19780503 |
| FR 2389597  | B1 | 19830819 |                |          |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| AU 7835733  | A1 | 19791108 | AU 1978-35733  | 19780503 |
| AU 517255   | B2 | 19810716 |                |          |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| CH 635570   | A  | 19830415 | CH 1978-4836   | 19780503 |
|             |    |          | LU 1977-77236  | 19770503 |
|             |    |          | LU 1977-77237  | 19770503 |
| JP 53141230 | A2 | 19781208 | JP 1978-53627  | 19780504 |
| JP 59040140 | B4 | 19840928 |                |          |
|             |    |          | LU 1977-77236  | 19770503 |



|            |   |          |               |          |
|------------|---|----------|---------------|----------|
| AT 7906288 | A | 19810715 | LU 1977-77237 | 19770503 |
| AT 366023  | B | 19820310 | AT 1979-6288  | 19790925 |
|            |   |          | LU 1977-77236 | 19770503 |
|            |   |          | LU 1977-77237 | 19770503 |
|            |   |          | AT 1978-3179  | 19780502 |

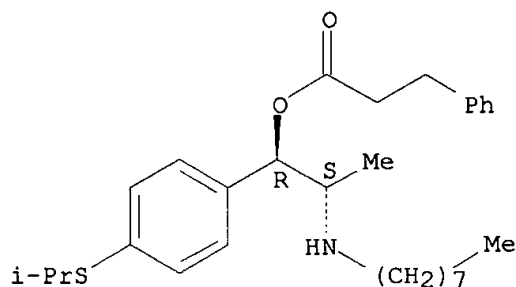
IT 69145-90-0

RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. as muscle relaxant)

RN 69145-90-0 CAPLUS

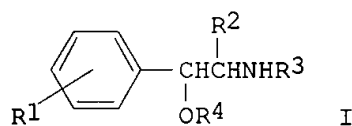
CN Benzenepropanoic acid, 1-[4-[(1-methylethyl)thio]phenyl]-2-(octylamino)propyl ester, hydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

GI



AB One hundred three amino alcs. I [R1 = H, C1-5 alkylthio, alkoxy, alkyl, C5-6 cycloalkylthio, cycloalkoxy, cycloalkyl, halo; R2 = C1-3 alkyl; R3 = C1-8 alkyl, C1-4 alkyl, optionally substituted with Ph, PhO, Bz, (un)substituted with alkyl, alkoxy, halo, C6-18 alkenyl, C5-9 cycloalkyl; R4 = COR5 [R5 = C1-10 alkyl, C2-4 alkenyl, C3-8 cycloalkyl, Ph (un)substituted with C1-3 alkyl, alkoxy, halo, C1-4 alkyl, (un)substituted with C1-3 carbalkoxy, alkoxy, NH2, acylamino, C5-6 cycloalkyl, PhO, Ph, optionally substituted with alkyl, alkoxy, halo, cinnamyl], H], useful as antihypertensives, peripheral vasodilators, muscle relaxants, platelet aggregation inhibitors, hypolipemics, and thrombosis inhibitors, were prepd. Thus, acylation of 4-Me2CHSC6H4CH(OH)CHMeNH(CH2)7Me by refluxing with AcCl in C6H6 or PrCOCl gave 70 or 52%, resp. of the corresponding 4-Me2CHSC6H4CH(OR4)CHMeNH(CH2)7Me (R4 = Ac, PrCO).

L4 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1973:147610 CAPLUS

DN 78:147610  
 TI Thiamphenicol phenylalaninate  
 IN Saiga, Akisuke; Yamanaka, Motosuke; Sato, Takashi  
 PA Eisai Co., Ltd.  
 SO Jpn. Kokai Tokkyo Koho, 2 pp.  
 CODEN: JKXXAF  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

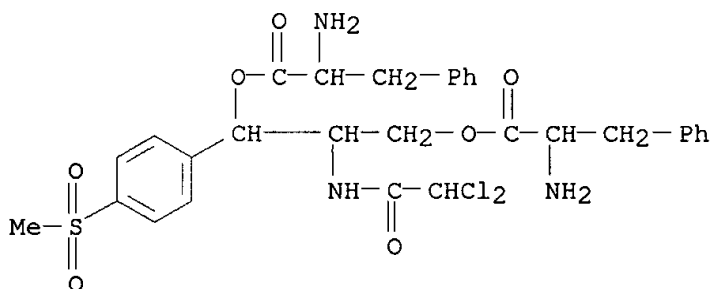
|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|-------------|------|----------|-----------------|----------|
| PI | JP 48004446 | B4   | 19730120 | JP 1971-27212   | 19710427 |

IT **41570-11-0P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

RN 41570-11-0 CAPLUS

CN L-Phenylalanine, 2-[(dichloroacetyl)amino]-1-[4-(methylsulfonyl)phenyl]-1,3-propanediyl ester, [R-(R\*,R\*)]- (9CI) (CA INDEX NAME)



AB A soln. of thiamphenicol and PhCH<sub>2</sub>CH(NH<sub>2</sub>)COCl.HCl (1:2 by mole) in anhyd. dioxane was stirred 7 hr at 13-17.degree. to give 61.2% thiamphenicol phenylalaninate, which was sol. and stable in H<sub>2</sub>O.

L4 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1970:67270 CAPLUS

DN 72:67270

TI Water soluble antibiotic chloramphenicol .beta.-phenylalanine ester salts

IN Zumin, Silva T.; Mosna, Sergio

PA Pierrel S.p.A.

SO Brit., 8 pp.

CODEN: BRXXAA

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | GB 1173562 |      | 19691210 | GB              | 19660425 |

IT **25613-59-6P 25613-62-1P 25613-63-2P**

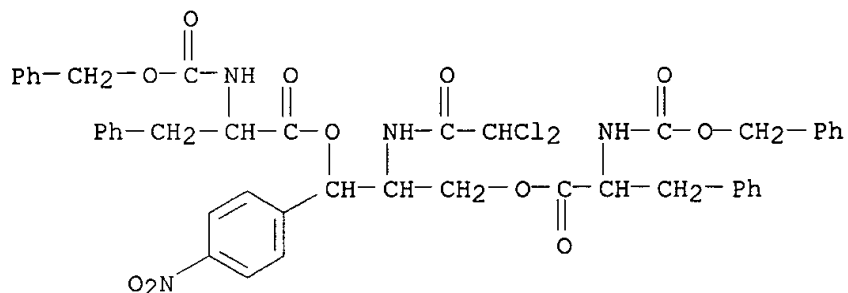
**25613-64-3P 25616-21-1P 25616-22-2P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

RN 25613-59-6 CAPLUS

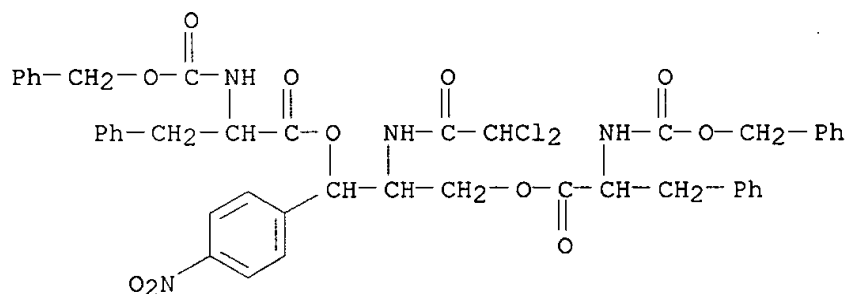
CN Alanine, N-carboxy-3-phenyl-, N-benzyl ester, L-, diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-

nitrophenethyl]acetamide (8CI) (CA INDEX NAME)



RN 25613-62-1 CAPLUS

Alanine, N-carboxy-3-phenyl-, N-benzyl ester, DL-, diester with  
D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-  
nitrophenethyl]acetamide (8CI) (CA INDEX NAME)



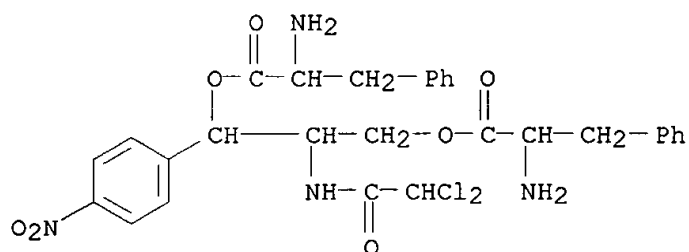
RN 25613-63-2 CAPLUS

CN Alanine, phenyl-, L-, diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide, bis(trifluoroacetate) (8CI) (CA INDEX NAME)

CM 1

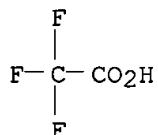
CRN 47832-98-4

CMF C29 H30 C12 N4 O7

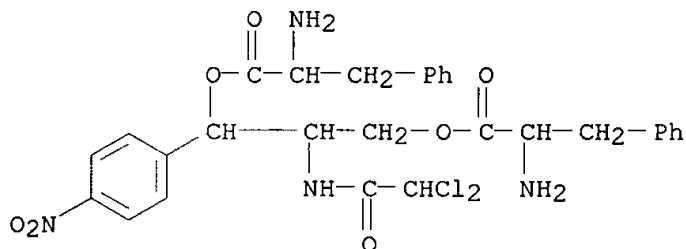


CM 2

CRN 76-05-1  
CMF C2 H F3 O2



RN 25613-64-3 CAPLUS  
CN Alanine, phenyl-, L-, diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide, dihydrochloride (8CI)  
(CA INDEX NAME)

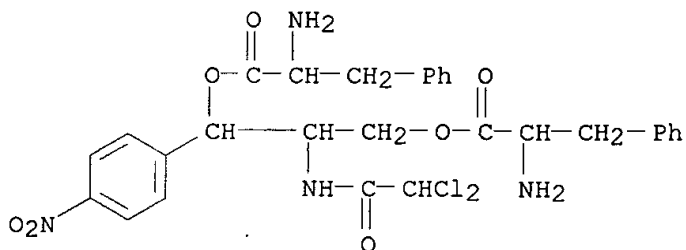


● 2 HCl

RN 25616-21-1 CAPLUS  
CN Alanine, N-acetyl-3-phenyl-, L-, compd. with L-phenylalanine diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide (2:1) (8CI) (CA INDEX NAME)

CM 1

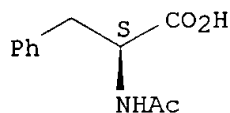
CRN 47832-98-4  
CMF C29 H30 Cl2 N4 O7



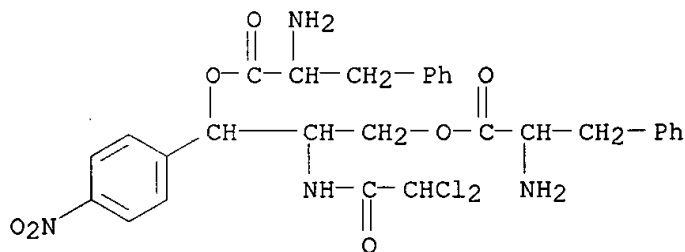
CM 2

CRN 2018-61-3  
CMF C11 H13 N O3

Absolute stereochemistry. Rotation (+).



RN 25616-22-2 CAPLUS  
CN Alanine, phenyl-, DL-, diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide, dihydrobromide (8CI)  
(CA INDEX NAME)

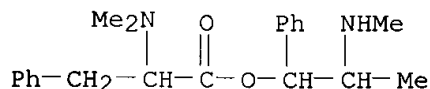


●2 HBr

AB Salts of chloramphenicol 1,3-bis(L-.beta.-phenylalaninate) (I) and chloramphenicol 3-L-.beta.-phenylalaninate (II), useful for parenteral administration, with antibiotic activity, were prepd. by reacting D-(-)-threo-1-p-nitrophenyl-2-dichloroacetamido-1,3-propanediol (chloramphenicol) (III) either with N-carbobenzoxyl-L-.beta.-phenylalanine (IV) in the presence of dicyclo-hexylcarbodiimide (V) and anhyd. pyridine (VI) or with IV anhydride (VII) in the presence of VI to give chloramphenicol 1,3-bis(N-carbobenzoxyl-L-.beta.-phenylalaninate) (VIII) and chloramphenicol 3-(N-carbobenzoxyl-L-.beta.-phenylalaninate) (IX), resp., followed by removal of the protecting group(s) by treatment with aq. HBr or anhyd. CF<sub>3</sub>CO<sub>2</sub>H. I and II are hydrolyzed in vivo to III and phenylalanine. Thus, addn. of 10.30 g V at 15.degree. to a stirred soln. of 29.93 g IV in 150 ml Me<sub>2</sub>CO, and the mixt. stirred 3 hr gave 96.5% VII. Racemic N-carbobenzoxyl-DL-.beta.-phenylalanine anhydride (X) (93.5%) was prepd. similarly. III (5.82 g) in 10 ml VI was added to 180 ml of an Me<sub>2</sub>CO soln. of 25.2 g VII and the mixt. stirred 5-6 hr at room temp. and poured on ice-HCl to give, after treatment with 3.5 ml p-H<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>NMe<sub>2</sub> (XI) in dry C<sub>6</sub>H<sub>6</sub> to remove excess VII, 90% VIII, m. 95-7.degree.. Racemic chloramphenicol 1,3-bis(N-carbobenzoxyl-.beta.-phenylalaninate) (XII) (94%), a yellow oil, was prepd. similarly from X. IV (22.45 g) and 15 ml VI added to a stirred soln. of 9.69 g III in 60 ml HCONMe<sub>2</sub>, the soln. cooled to -5 to -8.degree., 18.57 g V added slowly, the mixt. stirred 1 hr, kept 3 hr at -5.degree. and poured on a mixt. of 50 ml concd. HCl, 50 ml H<sub>2</sub>O, and 100 g ice gave a ppt., which was centrifuged off and extd.

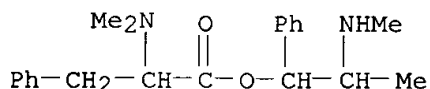
with C<sub>6</sub>H<sub>6</sub>. Treatment of the C<sub>6</sub>H<sub>6</sub> ext. with 3.5 ml XI gave 93% VIII, m. 95-7.degree.. IX, m. 145-7.degree., was prepd. similarly using 19.39 g III, 60 ml HCONMe<sub>2</sub>, 17.96 g IV, 15 ml VI, and 12.38 g V. A mixt. of 17.72 g VIII and 40 ml anhyd. CF<sub>3</sub>CO<sub>2</sub>H refluxed 1 hr in the presence of 8 g resorcinol gave 16.30 g I.CF<sub>3</sub>CO<sub>2</sub>H (XIII). Addn. of XIII to satd. aq. NaHCO<sub>3</sub>, extn. of the free base with CH<sub>2</sub>Cl<sub>2</sub>, and treatment of the ext. with HCl gave I.HCl, m. 220-222.degree. (decompn.). II.HCl, [.alpha.]<sub>D</sub> 10.77.degree. (c 2, H<sub>2</sub>O), was prepd. similarly from IX. A soln. of 5 g XII in 60 ml 2.5N HBr in AcOH stirred 10 min at 25 .degree. gave 85% a mixt. of chloramphenicol 1,3-bis(D- and L-.beta.-phenylalaninate-HBr) sep'd. by chromatog. XIII (13 g) treated with satd. aq. NaHCO<sub>3</sub>, extn. of the free base with CH<sub>2</sub>Cl<sub>2</sub>, and treatment of the ext. with N-acetyl-L-phenylalanine gave III 1,3-bis(L-.beta.-phenylalaninate N-acetyl-L-phenylalaninate); III 3-(L-.beta.-phenylalaninate N-acetyl-L-phenylalaninate) was prepd. similarly.

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2003 ACS  
 AN 1967:402830 CAPLUS  
 DN 67:2830  
 TI Separation of the organic bases by Craig partition. VII. Acyl migration in the stereoisomeric N-(N,N-dimethylphenylalanyl)ephedrines  
 AU Schoenenberger, Helmut; Fuchsberger, K. D.; Brinkmann, Rolf  
 CS Univ. Munich, Munich, Fed. Rep. Ger.  
 SO Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft (1967), 300(2), 126-35  
 CODEN: APBDAJ; ISSN: 0376-0367  
 DT Journal  
 LA German  
 IT **14355-01-2P 14355-02-3P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 14355-01-2 CAPLUS  
 CN Alanine, N,N-dimethyl-3-phenyl-, ester with (-)-pseudoephedrine, dihydrochloride, L- (8CI) (CA INDEX NAME)

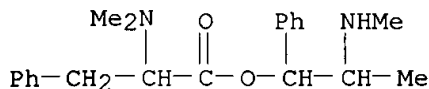


● 2 HCl

RN 14355-02-3 CAPLUS  
 CN Alanine, N,N-dimethyl-3-phenyl-, ester with (-)-pseudoephedrine, dihydrochloride, D- (8CI) (CA INDEX NAME)



2 HCl



● 2 HCl

AB cf. CA 66: 49281u. The compds. studied were N-(L-N,N-dimethylphenylalanyl)-L-ephedrine (I), N-(D-N,N-dimethylphenylalanyl)-L-ephedrine (II), N-(L-N,N-dimethylphenylalanyl)-L-pseudoephedrine (III), and N-(D-N,N-dimethylphenylalanyl)-L-pseudoephedrine (IV). In every case, only the ester of L-pseudoephedrine resulted, even under mild conditions (room temp., acetone-HCl). Complete inversion of the erythro derivs. occurred. In 2N HCl at 80.degree., the ester from I formed quant. in 10 min. while that from III (retention of configuration) required 25 hrs. With II, 5 hrs. and with IV, 22 hrs. were required. The 4 amides pass through either of 2 cyclic intermediates during the migration, L,L-(V) or D,L-pseudooxazolidine (VI). The rates are explained by steric considerations of the mechanism, V resulting from I via inversion and from III with retention, and VI, from II via inversion and IV with retention. Craig partition as described previously (loc. cit.) was used to sep. and det. the reaction products. Twenty-four partition steps using a solvent mixt. of 0.5M citrate buffer (pH 4/5)-MeOH-CHCl<sub>3</sub> (9:1:10 parts by vol.) were required for sepn. into N- and O-aminoacylphenedrines. The O-(L-N,N-dimethylphenylalanyl)-L-pseudoephedrine m. 170-2.degree., [ $\alpha$ ]<sub>D</sub><sup>20</sup> + 114.degree. (c = 0.0055 g./ml., 5N HCl) and the O-(D-N,N-dimethyl-) ester melts at 174-6.degree., [ $\alpha$ ]<sub>D</sub><sup>20</sup> 48.degree. (c 0.0055 g./ml., 5N HCl).

=> d cost

COST IN U.S. DOLLARS

| SINCE FILE          | TOTAL        |
|---------------------|--------------|
| ENTRY               | SESSION      |
| CONNECT CHARGES     | 0.34 0.83    |
| NETWORK CHARGES     | 0.06 0.18    |
| SEARCH CHARGES      | 0.00 147.75  |
| DISPLAY CHARGES     | 43.20 43.20  |
|                     | -----        |
|                     | 43.60 191.96 |
| CAPLUS FEE (5%)     | 2.18 2.18    |
|                     | -----        |
| FULL ESTIMATED COST | 45.78 194.14 |

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

| SINCE FILE          | TOTAL       |
|---------------------|-------------|
| ENTRY               | SESSION     |
| CA SUBSCRIBER PRICE | -6.51 -6.51 |

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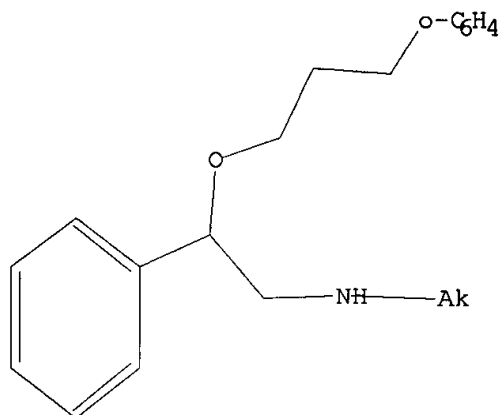
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L5 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

L1 STR



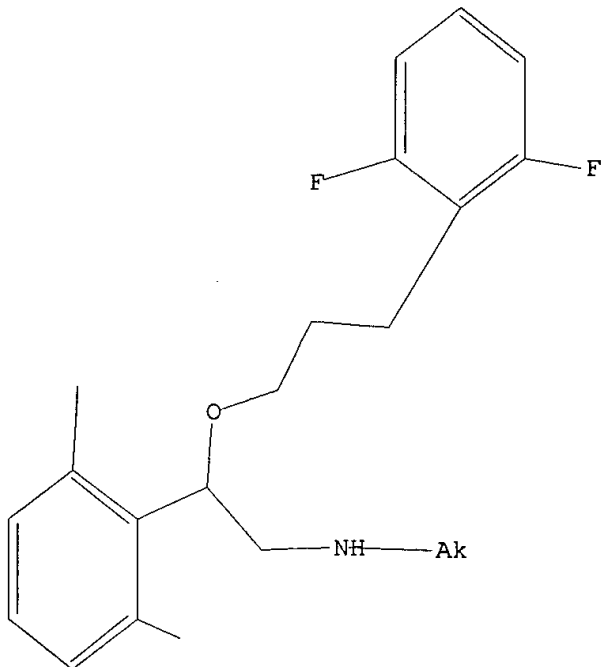
G1 NH,X,Hy

Structure attributes must be viewed using STN Express query preparation.

=> d 15

L5 HAS NO ANSWERS

L5 STR



G1 NH,X,Hy



Structure attributes must be viewed using STN Express query preparation.

=> s 15

**REGISTRY INITIATED**

Substance data SEARCH and crossover from CAS REGISTRY in progress...

Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 14:42:51 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS 0 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 2 TO 124  
PROJECTED ANSWERS: 0 TO 0

L6 0 SEA SSS SAM L5

L7 0 L6

=> s 15

**REGISTRY INITIATED**

Substance data SEARCH and crossover from CAS REGISTRY in progress...

Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 14:43:29 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS 0 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 2 TO 124  
PROJECTED ANSWERS: 0 TO 0

L8 0 SEA SSS SAM L5

L9 0 L8

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

|  | ENTRY      | SESSION |
|--|------------|---------|
| FULL ESTIMATED COST                        | 0.42       | 198.70  |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL   |
|  | ENTRY      | SESSION |
| CA SUBSCRIBER PRICE                        | 0.00       | -6.51   |

FILE 'REGISTRY' ENTERED AT 14:43:39 ON 26 MAY 2003  
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Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 25 MAY 2003 HIGHEST RN 519753-05-0  
DICTIONARY FILE UPDATES: 25 MAY 2003 HIGHEST RN 519753-05-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNote 27, Searching Properties  
in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> s 15

SAMPLE SEARCH INITIATED 14:43:43 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS 0 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 2 TO 124  
PROJECTED ANSWERS: 0 TO 0

L10 0 SEA SSS SAM L5

=> s 15 sss full

FULL SEARCH INITIATED 14:43:49 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 63 TO ITERATE

100.0% PROCESSED 63 ITERATIONS 19 ANSWERS  
SEARCH TIME: 00.00.01

L11 19 SEA SSS FUL L5

=> file caplu

|                      | SINCE FILE | TOTAL   |
|----------------------|------------|---------|
|                      | ENTRY      | SESSION |
| COST IN U.S. DOLLARS |            |         |
| FULL ESTIMATED COST  | 148.15     | 346.85  |

|  |            |         |
|--|------------|---------|
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL   |
|  | ENTRY      | SESSION |
| CA SUBSCRIBER PRICE                        | 0.00       | -6.51   |

FILE 'CAPLUS' ENTERED AT 14:43:55 ON 26 MAY 2003  
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FILE COVERS 1907 - 26 May 2003 VOL 138 ISS 22  
 FILE LAST UPDATED: 25 May 2003 (20030525/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l11

L12 1 L11

=> d l12 fbib hitstr abs total

L12 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

AN 2002:157723 CAPLUS

DN 136:216523

TI Preparation of phenylethanol(mono/di)amines and  
 phenylalkylethanol(mono/di)amines as sodium channel blockers

IN Fuchs, Klaus; Stransky, Werner; Grauert, Matthias; Carter, Adrian; Gaida,  
 Wolfram; Weiser, Thomas; Ensinger, Helmut

PA Boehringer Ingelheim Pharma K.-G., Germany

SO PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

|     | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|-----|---|------|----------|-----------------|----------|
|     | -----   | ---- | -----    | -----           | -----    |
| PI  | WO 2002016308   | A1   | 20020228 | WO 2001-EP9036  | 20010804 |
| W:  | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,<br>CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,<br>GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,<br>LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,<br>RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,<br>UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |          |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,<br>DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  |      |          |                 |          |

BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10040901 A1 20020314 DE 2000-10040901A 20000818  
 US 2002042410 A1 20020411 US 2001-912163 20010724  
 DE 2000-10040901A 20000818  
 US 2000-228675PP 20000829  
 AU 2001091737 A5 20020304 AU 2001-91737 20010804  
 DE 2000-10040901A 20000818  
 WO 2001-EP9036 W 20010804  
 EP 1311471 A1 20030521 EP 2001-971870 20010804  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
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 WO 2001-EP9036 W 20010804

OS MARPAT 136:216523

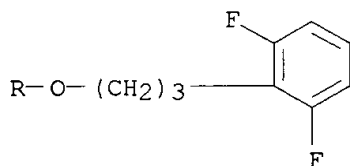
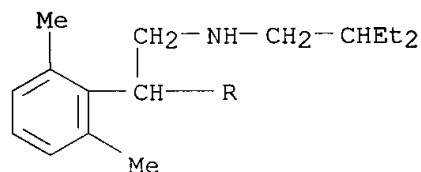
IT 401938-19-0P 401938-31-6P 401938-36-1P  
 401938-38-3P 401938-45-2P 401938-49-6P  
 401938-53-2P 401938-55-4P 401938-57-6P  
 401938-61-2P 401938-63-4P 401938-69-0P  
 401938-73-6P 401938-77-0P 401939-56-8P  
 401939-58-0P 401939-80-8P 401939-82-0P  
 401939-84-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(prepn. of phenylethanamines and phenylalkylethanamines as sodium  
 channel blockers)

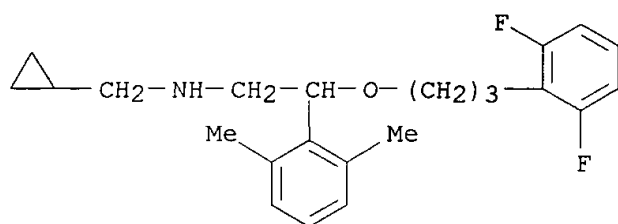
RN 401938-19-0 CAPLUS

CN Benzeneethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-N-(2-ethylbutyl)-  
 2,6-dimethyl- (9CI) (CA INDEX NAME)



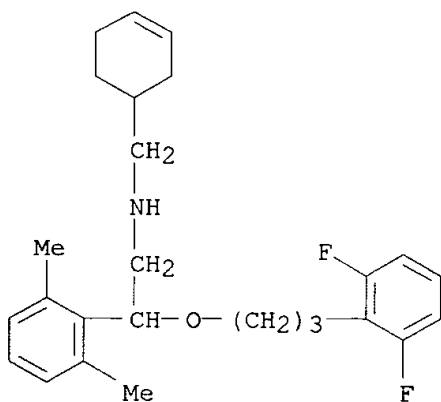
RN 401938-31-6 CAPLUS

CN Benzeneethanamine, N-(cyclopropylmethyl)-.beta.-[3-(2,6-  
 difluorophenyl)propoxy]-2,6-dimethyl- (9CI) (CA INDEX NAME)



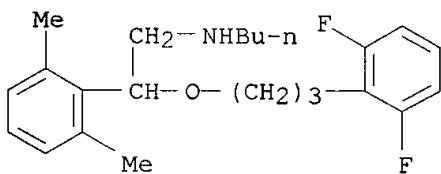
RN 401938-36-1 CAPLUS

CN Benzeneethanamine, N-(3-cyclohexen-1-ylmethyl)-.beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl- (9CI) (CA INDEX NAME)



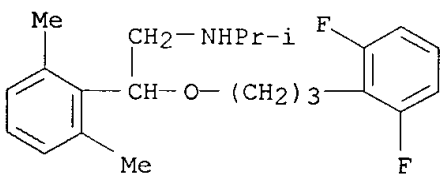
RN 401938-38-3 CAPLUS

CN Benzeneethanamine, N-butyl-.beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl- (9CI) (CA INDEX NAME)



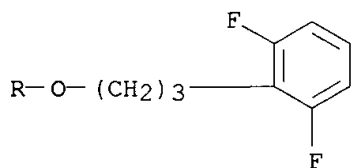
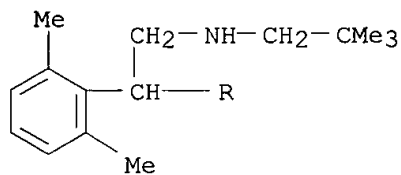
RN 401938-45-2 CAPLUS

CN Benzeneethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



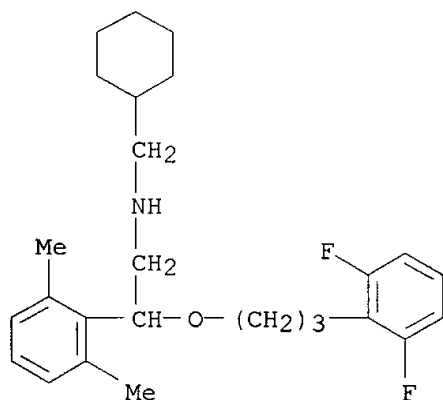
RN 401938-49-6 CAPLUS

CN Benzeneethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-N-(2,2-dimethylpropyl)-2,6-dimethyl- (9CI) (CA INDEX NAME)



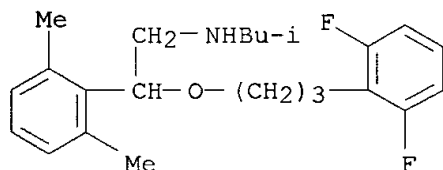
RN 401938-53-2 CAPLUS

CN Benzeneethanamine, N-(cyclohexylmethyl)-.beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl- (9CI) (CA INDEX NAME)



RN 401938-55-4 CAPLUS

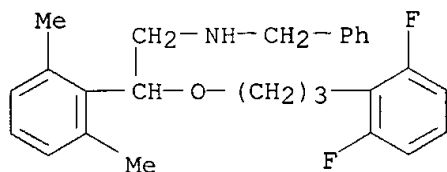
CN Benzeneethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 401938-57-6 CAPLUS

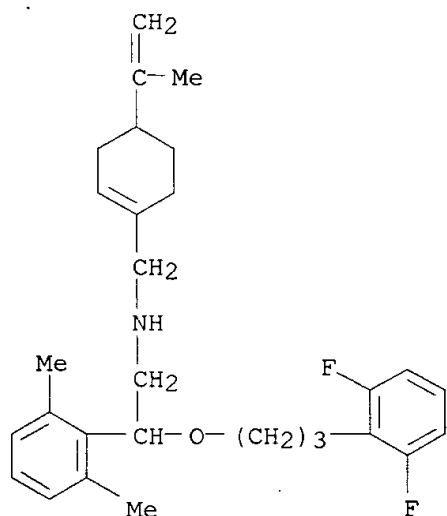
CN Benzeneethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-

(phenylmethyl)- (9CI) (CA INDEX NAME)



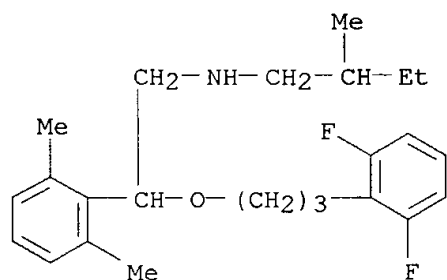
RN 401938-61-2 CAPLUS

CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-[[4-(1-methylethenyl)-1-cyclohexen-1-yl]methyl]- (9CI) (CA INDEX NAME)



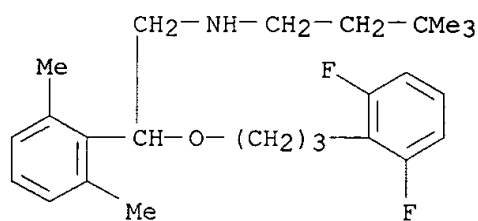
RN 401938-63-4 CAPLUS

CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-(2-methylbutyl)- (9CI) (CA INDEX NAME)



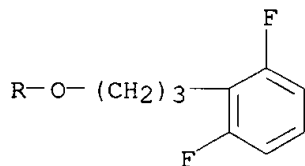
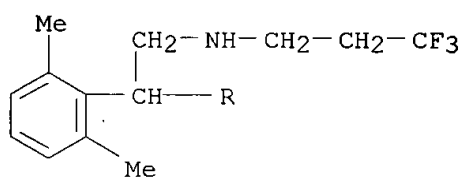
RN 401938-69-0 CAPLUS

CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-N-(3,3-dimethylbutyl)-2,6-dimethyl- (9CI) (CA INDEX NAME)



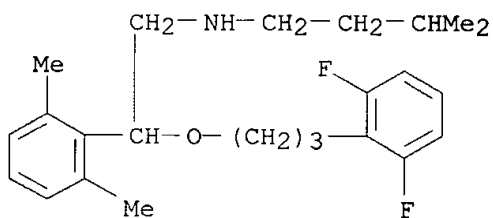
RN 401938-73-6 CAPLUS

CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-(3,3,3-trifluoropropyl)- (9CI) (CA INDEX NAME)



RN 401938-77-0 CAPLUS

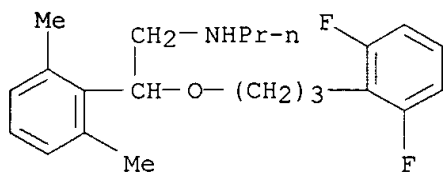
CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-(3-methylbutyl)- (9CI) (CA INDEX NAME)



RN 401939-56-8 CAPLUS

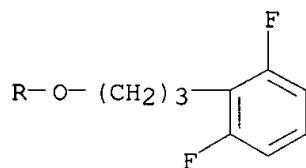
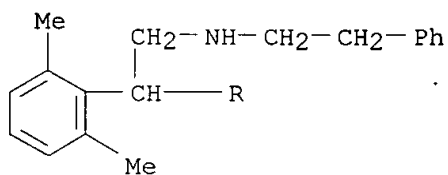
CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-propyl- (9CI) (CA INDEX NAME)





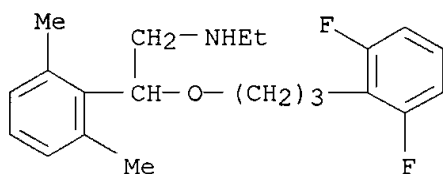
RN 401939-58-0 CAPLUS

CN Benzeneethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-(2-phenylethyl)- (9CI) (CA INDEX NAME)



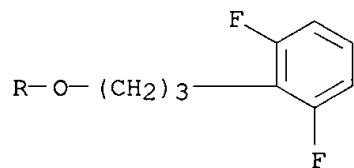
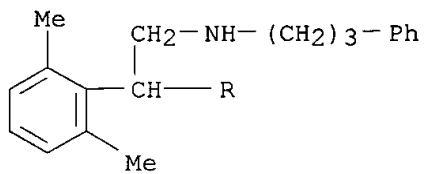
RN 401939-80-8 CAPLUS

CN Benzeneethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-N-ethyl-2,6-dimethyl- (9CI) (CA INDEX NAME)



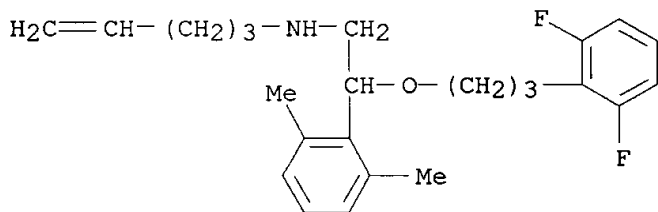
RN 401939-82-0 CAPLUS

CN Benzenepropanamine, N-[2-[3-(2,6-difluorophenyl)propoxy]-2-(2,6-dimethylphenyl)ethyl]- (9CI) (CA INDEX NAME)

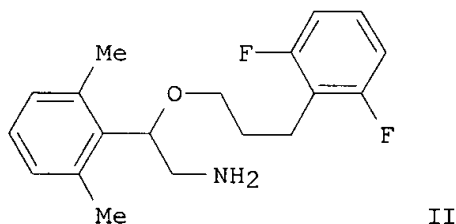
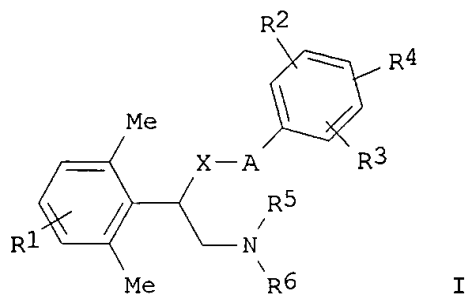


RN 401939-84-2 CAPLUS

CN Benzeneethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-4-pentenyl- (9CI) (CA INDEX NAME)



GI



AB Title compds. [I; R1 = OH, CF3, NO2, CN, halo, C1-8 alkyl, halo, C1-8 alkoxy; R2, R3, R4 independently = halo, C1-8 alkyl, OH, NO2, CN, C1-8 alkoxy, CF3; R5, R6 independently = C1-8 alkyl, C2-8 alkenyl, C3-8 alkynyl, C3-8 cycloalkyl, NH2, OH, O, COOH, CONH2; A = C1-5 alkylene, C2-4 alkenylene, C3-4 alkylene; X = NH, N(CHO), halo, O, etc.] are prepd. The invention further relates to a method for producing said compds. and to their compn. in use as medicaments. Title compds. I are used as blockers of the voltage-dependent sodium channel and can be used for diseases that are assocd. with a functional disorder caused by hyperexcitability. Thus, the title compd. II was prepd. from trifluoroacetic anhydride, 2,6-dimethylbenzaldehyde, which was prepd. from 2-bromo-3-dimethylbenzene, and 2-(3-bromopropyl)-1,3-difluorobenzene, which was prepd. from di-Et malonate and 2,6-difluorobenzyl bromide.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d cost

COST IN U.S. DOLLARS

|                     | SINCE FILE<br>ENTRY | TOTAL<br>SESSION |
|---------------------|---------------------|------------------|
| CONNECT CHARGES     | 0.34                | 5.25             |
| NETWORK CHARGES     | 0.06                | 0.96             |
| SEARCH CHARGES      | 0.00                | 295.50           |
| DISPLAY CHARGES     | 4.32                | 47.52            |
|                     | -----               | -----            |
|                     | 4.72                | 349.23           |
| CAPLUS FEE (5%)     | 0.23                | 2.57             |
|                     | -----               | -----            |
| FULL ESTIMATED COST | 4.95                | 351.80           |

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

SINCE FILE

ENTRY

-0.65

TOTAL

SESSION

0 -7.16

IN FILE 'CAPLUS' AT 14:44:22 ON 26 MAY 2003

Welcome to STN International! Enter x:x

LOGINID:sssptal611sxp

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2 Apr 08 "Ask CAS" for self-help around the clock  
NEWS 3 Jun 03 New e-mail delivery for search results now available  
NEWS 4 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN  
NEWS 5 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)  
now available on STN  
NEWS 6 Aug 26 Sequence searching in REGISTRY enhanced  
NEWS 7 Sep 03 JAPIO has been reloaded and enhanced  
NEWS 8 Sep 16 Experimental properties added to the REGISTRY file  
NEWS 9 Sep 16 CA Section Thesaurus available in CAPLUS and CA  
NEWS 10 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985  
NEWS 11 Oct 24 BEILSTEIN adds new search fields  
NEWS 12 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN  
NEWS 13 Nov 18 DKILIT has been renamed APOLLIT  
NEWS 14 Nov 25 More calculated properties added to REGISTRY  
NEWS 15 Dec 04 CSA files on STN  
NEWS 16 Dec 17 PCTFULL now covers WP/PCT Applications from 1978 to date  
NEWS 17 Dec 17 TOXCENTER enhanced with additional content  
NEWS 18 Dec 17 Adis Clinical Trials Insight now available on STN  
NEWS 19 Jan 29 Simultaneous left and right truncation added to COMPENDEX,  
ENERGY, INSPEC  
NEWS 20 Feb 13 CANCERLIT is no longer being updated  
NEWS 21 Feb 24 METADEX enhancements  
NEWS 22 Feb 24 PCTGEN now available on STN  
NEWS 23 Feb 24 TEMA now available on STN  
NEWS 24 Feb 26 NTIS now allows simultaneous left and right truncation  
NEWS 25 Feb 26 PCTFULL now contains images  
NEWS 26 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results  
NEWS 27 Mar 20 EVENTLINE will be removed from STN  
NEWS 28 Mar 24 PATDPAFULL now available on STN  
NEWS 29 Mar 24 Additional information for trade-named substances without  
structures available in REGISTRY  
NEWS 30 Apr 11 Display formats in DGENE enhanced  
NEWS 31 Apr 14 MEDLINE Reload  
NEWS 32 Apr 17 Polymer searching in REGISTRY enhanced  
NEWS 33 Apr 21 Indexing from 1947 to 1956 being added to records in CA/CAPLUS  
NEWS 34 Apr 21 New current-awareness alert (SDI) frequency in  
WPIDS/WPINDEX/WPIX  
NEWS 35 Apr 28 RDISCLOSURE now available on STN  
NEWS 36 May 05 Pharmacokinetic information and systematic chemical names  
added to PHAR  
NEWS 37 May 15 MEDLINE file segment of TOXCENTER reloaded  
NEWS 38 May 15 Supporter information for ENCOMPPAT and ENCOMPLIT updated  
NEWS 39 May 16 CHEMREACT will be removed from STN

NEWS 40 May 19 Simultaneous left and right truncation added to WSCA  
NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and  
right truncation

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT  
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),  
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003  
NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS INTER General Internet Information  
NEWS LOGIN Welcome Banner and News Items  
NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that  
specific topic.

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of commercial gateways or other similar uses is prohibited and may  
result in loss of user privileges and other penalties.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 15:16:37 ON 26 MAY 2003

=> file reg

| COST IN U.S. DOLLARS | SINCE FILE<br>ENTRY | TOTAL<br>SESSION |
|----------------------|---------------------|------------------|
| FULL ESTIMATED COST  | 0.21                | 0.21             |

FILE 'REGISTRY' ENTERED AT 15:16:42 ON 26 MAY 2003

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Property values tagged with IC are from the ZIC/VINITI data file  
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STRUCTURE FILE UPDATES: 25 MAY 2003 HIGHEST RN 519753-05-0  
DICTIONARY FILE UPDATES: 25 MAY 2003 HIGHEST RN 519753-05-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNote 27, Searching Properties  
in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>

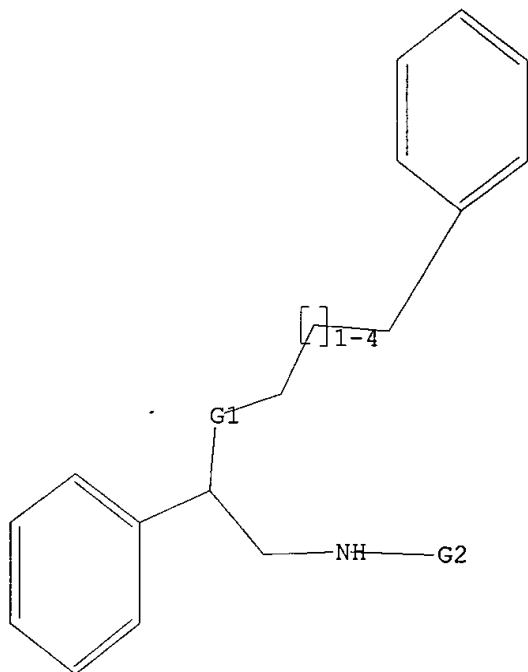
Uploading 09912163.4

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



G1 C,O,N,NH

G2 Cy,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 15:17:18 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 13957 TO ITERATE

7.2% PROCESSED 1000 ITERATIONS  
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)  
SEARCH TIME: 00.00.01

1 ANSWERS

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 272072 TO 286208

PROJECTED ANSWERS: 55 TO 503

L2 1 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 15:17:25 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 280434 TO ITERATE

100.0% PROCESSED 280434 ITERATIONS  
SEARCH TIME: 00.00.13

436 ANSWERS

L3 436 SEA SSS FUL L1

=&gt; file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

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148.76

FILE 'CAPLUS' ENTERED AT 15:17:45 ON 26 MAY 2003

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FILE COVERS 1907 - 26 May 2003 VOL 138 ISS 22

FILE LAST UPDATED: 25 May 2003 (20030525/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=&gt; s l3

L4 148 L3

=&gt; s l4 and overstimulation

L5 0 L4 AND OVERSTIMULATION

=&gt; s l4 and neurodegeneration

L6 0 L4 AND NEURODEGENERATION

=&gt; s l4 and AD

L7 0 L4 AND AD

=&gt; s l4 and stroke

L8 0 L4 AND STROKE

=&gt; d l4 fbib hitstr abs total

L4 ANSWER 1 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 2002:849669 CAPLUS

DN 137:346158

TI Pentapeptide compounds, their preparation, and their use

IN Doronina, Svetlana; Senter, Peter D.; Toki, Brian E.

PA Seattle Genetics, Inc., USA

SO PCT Int. Appl., 161 pp.



CODEN: PIXXD2

DT Patent

LA English

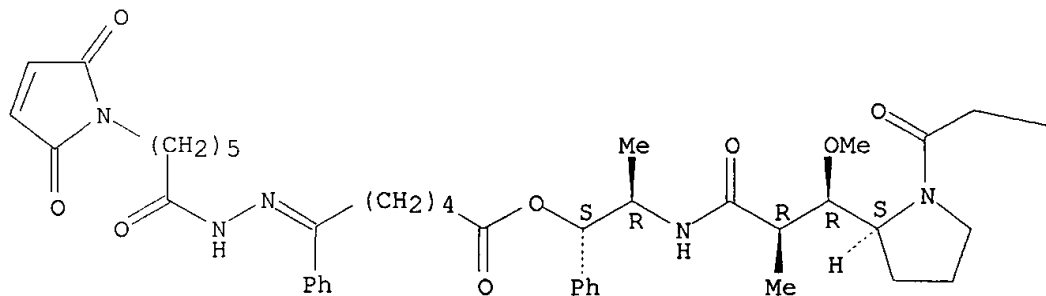
FAN.CNT 1

|    | PATENT NO.   | KIND   | DATE     | APPLICATION NO.  | DATE     |
|----|--|--|----------|------------------|----------|
| PI | WO 2002088172  | A2   | 20021107 | WO 2002-US13435  | 20020430 |
|    | WO 2002088172  | A3   | 20030227 |                  |          |
|    | W:   | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                  |          |
|    | RW:  | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                  |          |
|    |  |  |          | US 2001-845786 A | 20010430 |
|    |  |  |          | US 2001-1191 A   | 20011101 |
|    | US 2003083263  | A1   | 20030501 | US 2001-845786   | 20010430 |
| OS | MARPAT 137:346158  |  |          |                  |          |
| IT | 474645-11-9DP, monoclonal antibody conjugates  |  |          |                  |          |
|    | RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)   |  |          |                  |          |
|    | (pentapeptide compd. prepn. and use)   |  |          |                  |          |
| RN | 474645-11-9 CAPLUS   |  |          |                  |          |
| CN | L-Valinamide, N,N-dimethyl-L-valyl-N-[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[[[(1R,2S)-2-[[[6-[[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]hydrazono]-1-oxo-6-phenylhexyl]oxy]-1-methyl-2-phenylethyl]amino]-1-methoxy-2-methyl-3-oxopropyl]-1-pyrrolidinyl]-2-methoxy-1-[(1S)-1-methylpropyl]-4-oxobutyl]-N-methyl- (9CI) (CA INDEX NAME) |  |          |                  |          |

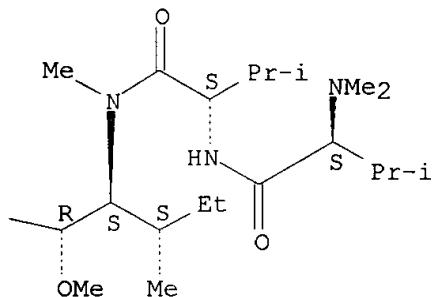
Absolute stereochemistry.

Double bond geometry unknown.

PAGE 1-A



PAGE 1-B



IT 474645-11-9 474645-18-6

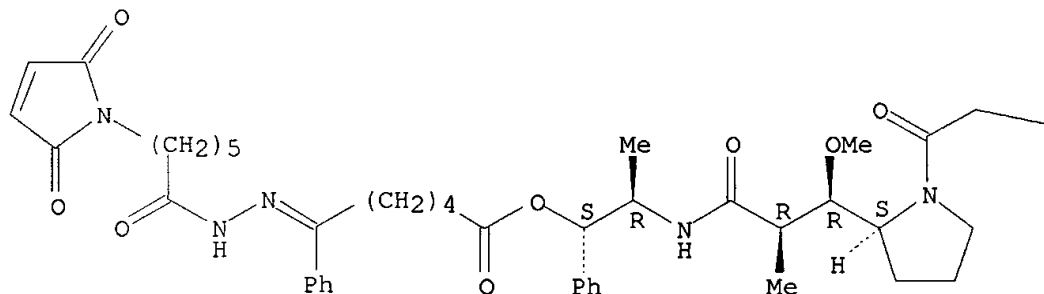
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(pentapeptide compd. prepn. and use)

RN 474645-11-9 CAPLUS

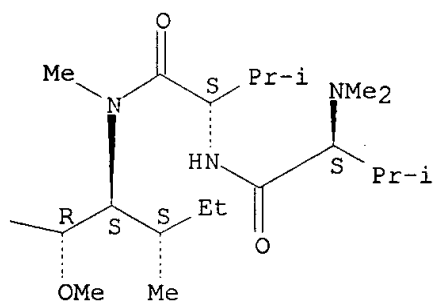
CN L-Valinamide, N,N-dimethyl-L-valyl-N-[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-  
[[ (1R,2S)-2-[[6-[[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-  
oxohexyl]hydrazono]-1-oxo-6-phenylhexyl]oxy]-1-methyl-2-phenylethyl]amino]-  
1-methoxy-2-methyl-3-oxopropyl]-1-pyrrolidinyl]-2-methoxy-1-[(1S)-1-  
methylpropyl]-4-oxobutyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.

PAGE 1-A



PAGE 1-B

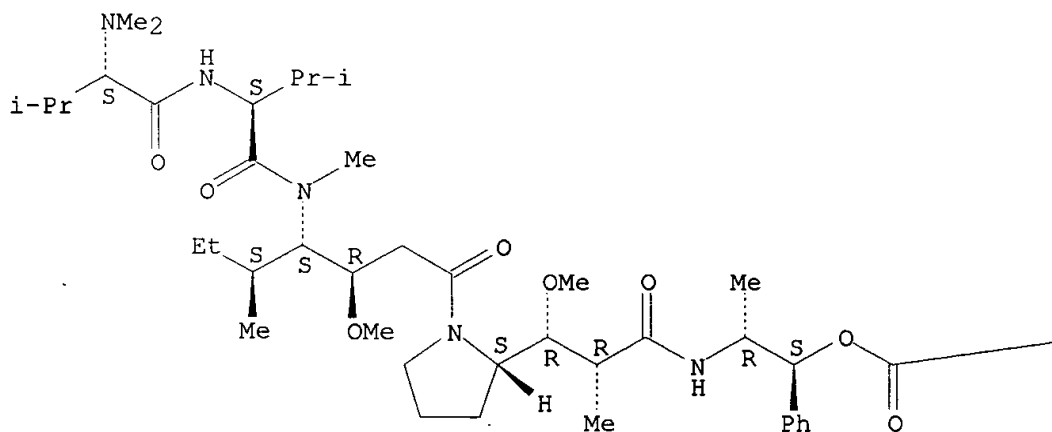


RN 474645-18-6 CAPLUS

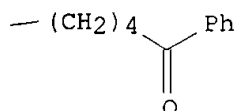
CN L-Valinamide, N,N-dimethyl-L-valyl-N-[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[[ (1R,2S)-2-[(1,6-dioxo-6-phenylhexyl)oxy]-1-methyl-2-phenylethyl]amino]-1-methoxy-2-methyl-3-oxopropyl]-1-pyrrolidinyl]-2-methoxy-1-[(1S)-1-methylpropyl]-4-oxobutyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 474645-11-9DP, mercaptoethanol adducts

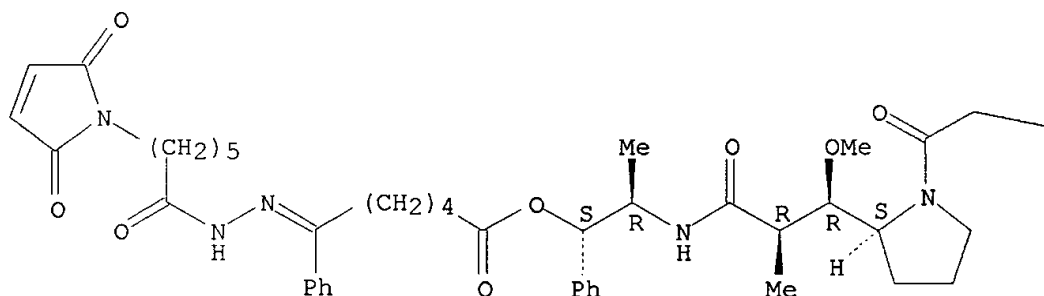
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(pentapeptide compd. prepn. and use)

RN 474645-11-9 CAPLUS

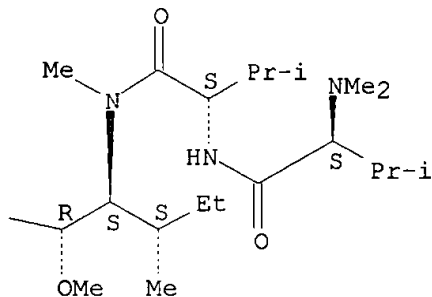
CN L-Valinamide, N,N-dimethyl-L-valyl-N-[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-  
[[[(1R,2S)-2-[[6-[[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-  
oxohexyl]hydrazono]-1-oxo-6-phenylhexyl]oxy]-1-methyl-2-phenylethyl]amino]-  
1-methoxy-2-methyl-3-oxopropyl]-1-pyrrolidinyl]-2-methoxy-1-[(1S)-1-  
methylpropyl]-4-oxobutyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.

PAGE 1-A



PAGE 1-B



AB Pentapeptide compds. are disclosed. The compds. have biol. activity, e.g., cytotoxicity. Prodrugs having targeting groups and pentapeptide moieties, as well as precursors thereof are also disclosed. For example, precursors having a reactive linker that can serve as a reaction site for joining to a targeting agent, e.g., an antibody, as disclosed. Prepn. of compds. of the invention is described.

L4 ANSWER 2 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 2002:805207 CAPLUS

DN 138:153819

TI Novel peptide-heterocycle hybrids: Synthesis and preliminary studies on calpain inhibition

AU Mann, Enrique; Chana, Antonio; Sanchez-Sancho, Francisco; Puerta, Carmen;  
Garcia-Merino, Antonio; Herradon, Bernardo

CS Instituto de Quimica Organica General, C.S.I.C., Juan de la Cierva 3,  
Madrid, 28006, Spain

SO Advanced Synthesis & Catalysis (2002), 344(8), 855-867

CODEN: ASCAF7; ISSN: 1615-4150

PB Wiley-VCH Verlag GmbH & Co. KGaA

DT Journal

LA English

IT 496803-30-6P

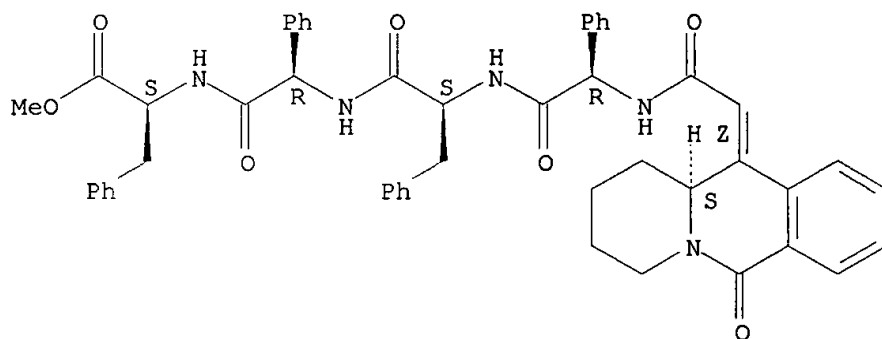
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. of oligopeptide-heterocycle conjugates as calpain inhibition agents)

RN 496803-30-6 CAPLUS

CN L-Phenylalanine, (2R)-2-phenyl-N-[(2Z)-[(11aS)-1,3,4,11a-tetrahydro-6-oxo-2H-benzo[b]quinolizin-11(6H)-ylidene]acetyl]glycyl-L-phenylalanyl-(2R)-2-phenylglycyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



IT 496802-68-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of oligopeptide-heterocycle conjugates as calpain inhibition agents)

RN 496802-68-7 CAPLUS

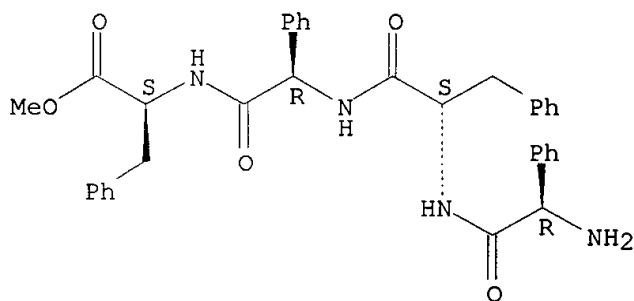
CN L-Phenylalanine, (2R)-2-phenylglycyl-L-phenylalanyl-(2R)-2-phenylglycyl-, methyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 496802-67-6

CMF C35 H36 N4 O5

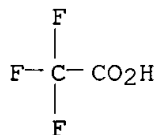
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



AB New peptidic compds., having peptide chains linked to bi- and tricyclic heterocycles (peptide-heterocycle hybrids), have been synthesized. The

heterocyclic components are derivs. of partially reduced isoquinoline and pyrido[1,2-b]isoquinoline bearing .alpha.,.beta.-unsatd. carbonyl functionalities. The heterocyclic compds. have been used as acylating agents in coupling reactions with short N-unprotected peptides. Based on our interest on potential calpain inhibitors, we have used short (2-4 amino acids) peptides with hydrophobic amino acids of the two enantiomeric series. We report preliminary studies on the inhibition of calpain, with some compds. having IC50 values in the nanomolar range.

RE.CNT 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 2002:671743 CAPLUS

DN 137:201608

TI Synthesis of antibacterial siderophore-amino acid/peptide-antibiotic conjugates for therapeutic use

IN Wittmann, Steffen; Heinisch, Lothar; Mollmann, Ute

PA Grunenthal GmbH, Germany

SO Ger. Offen., 10 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

|    | PATENT NO.    | KIND   | DATE     | APPLICATION NO.   | DATE     |
|----|---------------|--|----------|-------------------|----------|
| PI | DE 10111163   | A1   | 20020905 | DE 2001-10111163  | 20010301 |
|    | WO 2002070017 | A1   | 20020912 | WO 2002-EP2074    | 20020227 |
|    | W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                   |          |
|    | RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                   |          |
|    |               |  |          | DE 2001-10111163A | 20010301 |

OS MARPAT 137:201608

IT **439152-40-6P 454472-75-4P**

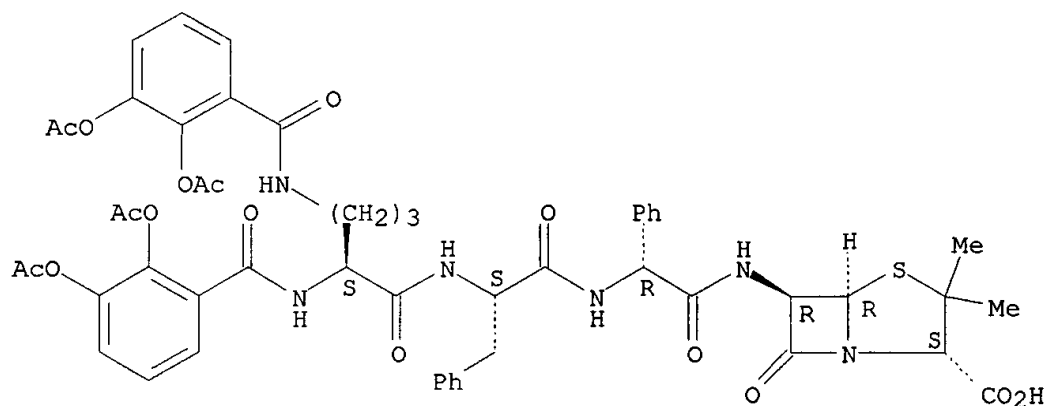
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of for use as antibacterial agents)

RN 439152-40-6 CAPLUS

CN Glycinamide, N2,N5-bis[2,3-bis(acetyloxy)benzoyl]-L-ornithyl-L-phenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)

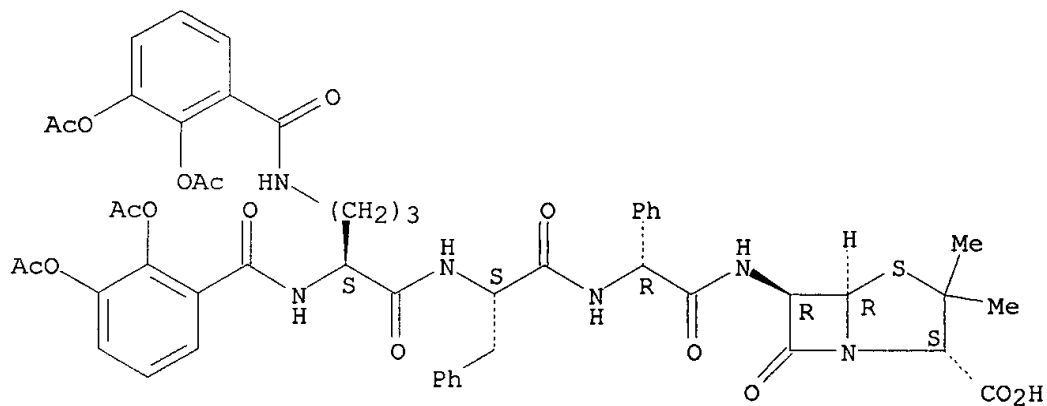
Absolute stereochemistry.



RN 454472-75-4 CAPLUS

CN Glycinamide, N2,N5-bis[2,3-bis(acetyloxy)benzoyl]-L-ornithyl-L-phenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, monosodium salt, (2R)- (9CI) (CA INDEX NAME)

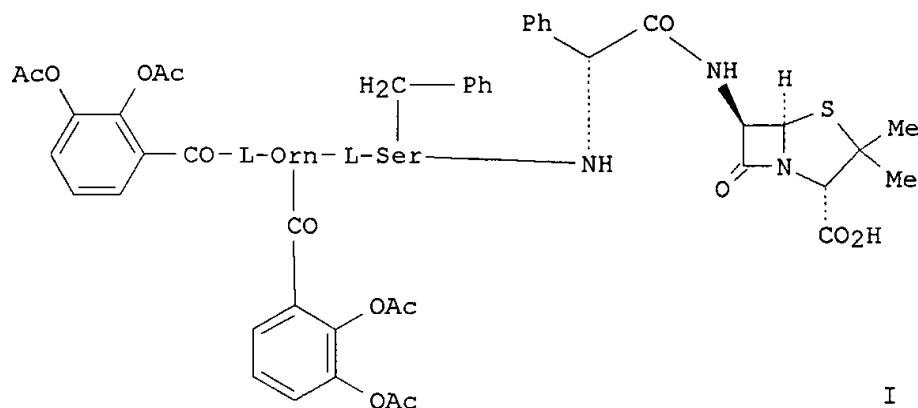
Absolute stereochemistry.



● Na

GI





AB The invention concerns siderophore-amino acid/peptide-antibiotic conjugates (e.g., I) capable of utilizing the bacterial iron transport mechanism for use as antibacterial agents. Thus, I was prepd. by condensation of N-[N2,N5-bis(2,3-diacetoxybenzoyl)-L-ornithinyl]-L-O-benzyl-serine and ampicillin, with further reaction to prep. the sodium salt. In antibacterial tests against a panel of organisms, title compds. had activities comparable or better than azlocillin, ampicillin, or meropenem.

L4 ANSWER 4 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 2002:588657 CAPLUS

DN 138:165595

TI Biomimetic synthesis and optimization of cyclic peptide antibiotics

AU Kohli, Rahul M.; Walsh, Christopher T.; Burkart, Michael D.

CS Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA, 02115, USA

SO Nature (London, United Kingdom) (2002), 418(6898), 658-661  
CODEN: NATUAS; ISSN: 0028-0836

PB Nature Publishing Group

DT Journal

LA English

IT **484014-59-7D**, immobilized, on polyethylene glycol amide resin

**484014-60-0D**, immobilized, on polyethylene glycol amide resin

RL: CRG (Combinatorial reagent); RGT (Reagent); CMBI (Combinatorial study); RACT (Reactant or reagent)

(biomimetic synthesis and optimization of cyclic peptide antibiotics)

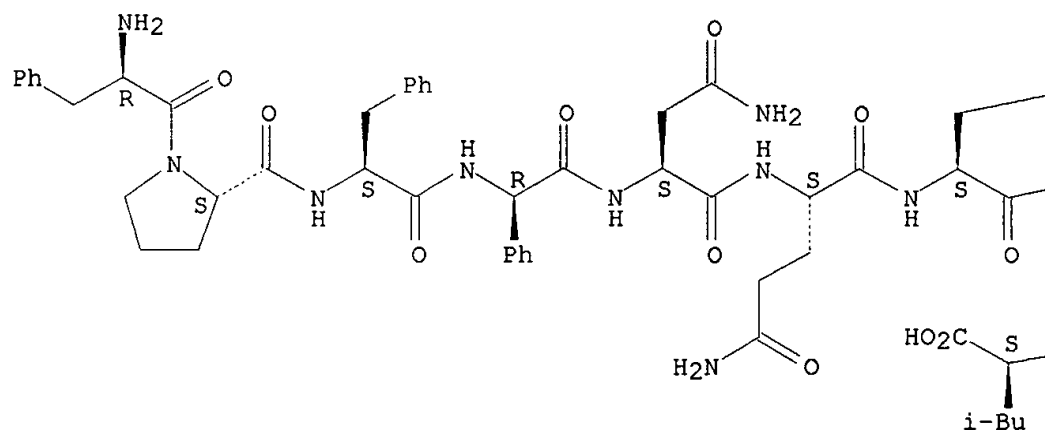
RN 484014-59-7 CAPLUS

CN L-Leucine, D-phenylalanyl-L-prolyl-L-phenylalanyl-(2S)-2-phenylglycyl-L-asparaginyl-L-glutaminyl-L-tyrosyl-L-valyl-L-ornithyl- (9CI) (CA INDEX NAME)

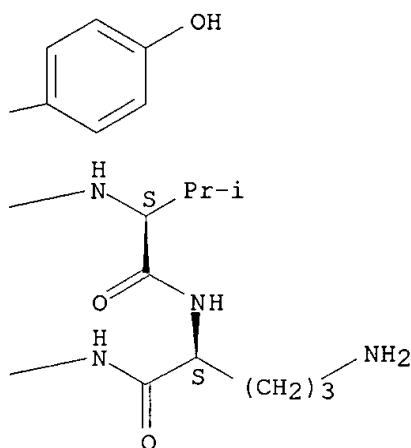
Absolute stereochemistry.



PAGE 1-A



PAGE 1-B



AB Mols. in nature are often brought to a bioactive conformation by ring formation (macrocyclization). A recurrent theme in the enzymic synthesis of macrocyclic compds. by non-ribosomal and polyketide synthetases is the tethering of activated linear intermediates through thioester linkages to carrier proteins, in a natural analogy to solid-phase synthesis. A terminal thioesterase domain of the synthetase catalyzes release from the tether and cyclization. Here we show that an isolated thioesterase can catalyze the cyclization of linear peptides immobilized on a solid-phase support modified with a biomimetic linker, offering the possibility of merging natural-product biosynthesis with combinatorial solid-phase chem. Starting from the cyclic decapeptide antibiotic tyrocidine A, this chemoenzymic approach allows us to diversify the linear peptide both to probe the enzymol. of the macrocyclizing enzyme, TycC thioesterase, and to create a library of cyclic peptide antibiotic products. We have used this method to reveal natural-product analogs of potential therapeutic utility; these compds. have an increased preference for bacterial over eukaryotic

membranes and an improved spectrum of activity against some common bacterial pathogens.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 148 CAPLUS COPYRIGHT 2003 ACS  
AN 2002:540135 CAPLUS  
DN 137:108295  
TI Vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases  
IN Chalifour, Robert; Hebert, Lise; Kong, Xianqi; Gervais, Francine  
PA Can.  
SO U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 724,842.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 2

| PATENT NO.   | KIND | DATE     | APPLICATION NO.   | DATE     |
|--|------|----------|-------------------|----------|
| PI US 2002094335   | A1   | 20020718 | US 2001-867847    | 20010529 |
|  |      |          | US 1999-168594PP  | 19991129 |
|  |      |          | US 2000-724842 A2 | 20001128 |
| WO 2002096937  | A2   | 20021205 | WO 2002-CA763     | 20020529 |
| W:   |      |          |                   |          |
| AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                   |          |
| RW:  |      |          |                   |          |
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|  |      |          | US 2001-867847 A  | 20010529 |

# PATENT FAMILY INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO.  | DATE     |
|--|------|----------|------------------|----------|
| FAN 2001:416788  |      |          |                  |          |
| PI WO 2001039796   | A2   | 20010607 | WO 2000-CA1413   | 20001129 |
| WO 2001039796  | A3   | 20011206 |                  |          |
| W:   |      |          |                  |          |
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| RW:  |      |          |                  |          |
| GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |      |          |                  |          |
|  |      |          | US 1999-168594PP | 19991129 |
|  |      |          | US 2000-724842 A | 20001128 |
| BR 2000016022  | A    | 20020806 | BR 2000-16022    | 20001129 |
|  |      |          | US 1999-168594PP | 19991129 |
|  |      |          | US 2000-724842 A | 20001128 |
|  |      |          | WO 2000-CA1413 W | 20001129 |
| EP 1235587   | A2   | 20020904 | EP 2000-981111   | 20001129 |
| R:   |      |          |                  |          |
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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 1999-168594PP 19991129  
 US 2000-724842 A 20001128  
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 US 2000-724842 A 20001128  
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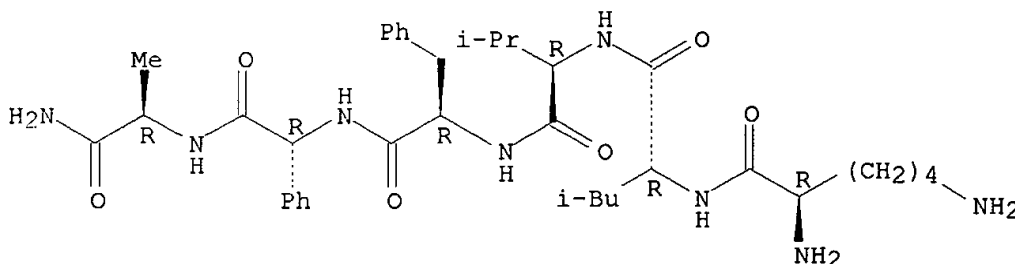
IT 342878-09-5

RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccines comprising all-D fibril peptides for prevention and treatment  
 of Alzheimer's and amyloid-related diseases)

RN 342878-09-5 CAPLUS

CN D-Alaninamide, D-lysyl-D-leucyl-D-valyl-D-phenylalanyl-(2R)-2-phenylglycyl-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The present invention relates to a stereochem. based "non-self" antigen vaccine for the prevention and/or treatment of Alzheimer's and other amyloid related diseases. The present invention provides a vaccine for the prevention and treatment of Alzheimer's and other amyloid related diseases, which overcomes the drawbacks assocd. with using naturally occurring peptides, proteins or immunogens. The vaccine comprises fibril peptides consisting of all- D-amino acids.

L4 ANSWER 6 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 2002:311304 CAPLUS

DN 137:149471

TI New CSPs based on peptidomimetics: efficient chiral selectors in  
 enantioselective separations

AU Burguete, M. Isabel; Frechet, Jean M. J.; Garcia-Verdugo, Eduardo; Janco,  
 Miroslav; Luis, Santiago V.; Svec, Frantisek; Vicent, Maria J.; Xu,  
 Mingcheng

CS Department of Inorganic and Organic Chemistry, E.S.T.C.E. Universitat  
 Jaume I, Castellon, E-12080, Spain

SO Polymer Bulletin (Berlin, Germany) (2002), 48(1), 9-15

CODEN: POBUDR; ISSN: 0170-0839

PB Springer-Verlag

DT Journal

LA English

IT 253426-92-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

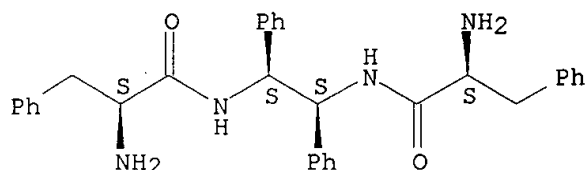
(in prepn. of chiral stationary phases based on peptidomimetics for

enantioselective sepn.)

RN 253426-92-5 CAPLUS

CN Benzenepropanamide, N,N'-[(1S,2S)-1,2-diphenyl-1,2-ethanediyl]bis[.alpha.-amino-, (.alpha.S,.alpha.'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 444647-79-4P

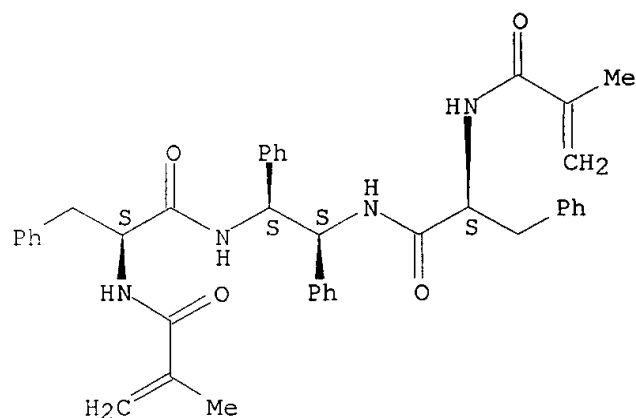
RL: ARU (Analytical role, unclassified); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent)

(peptidomimetics; prepn. of chiral stationary phases based on peptidomimetics for enantioselective sepn.)

RN 444647-79-4 CAPLUS

CN Benzenepropanamide, N,N'-[(1S,2S)-1,2-diphenyl-1,2-ethanediyl]bis[.alpha.-[(2-methyl-1-oxo-2-propenyl)amino]-, (.alpha.S,.alpha.'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



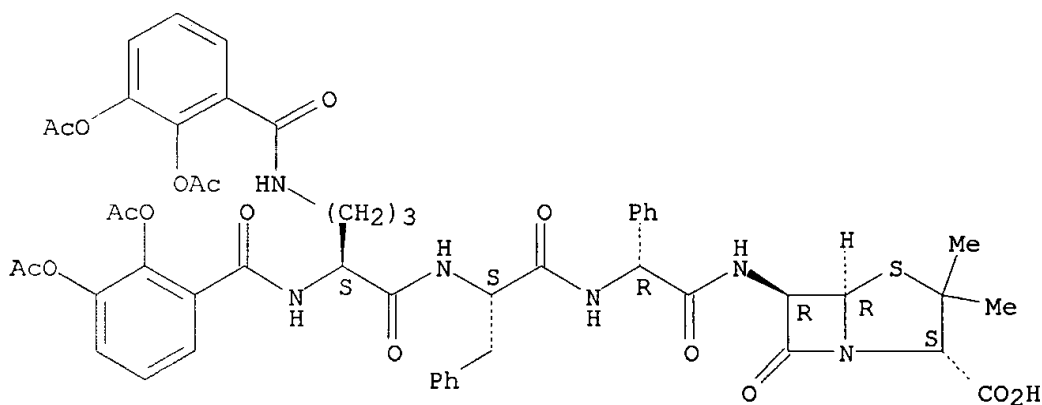
AB Two different families of peptidomimetics were synthesized and used as chiral selectors for enantioselective chromatog. The functionalization of compds. with multiple nitrogen atoms allows their use in the prepn. of chiral stationary phases (CSPs), with acrylic or styryl comonomers, in both bead and monolithic formats. Some of these sepn. media, having the appropriate morphol. properties for their use in chromatog. columns, were able to efficiently discriminate enantiomers of amino acid derivs. and pharmaceuticals such as oxazepam.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 2002:251248 CAPLUS  
 DN 137:60114  
 TI New synthetic siderophores and their .beta.-lactam conjugates based on diamino acids and dipeptides  
 AU Wittmann, S.; Schnabelrauch, M.; Scherlitz-Hofmann, I.; Mollmann, U.; Ankel-Fuchs, D.; Heinisch, L.  
 CS Hans Knoll Institute for Natural Product Research, Jena, Jena, D-07745, Germany  
 SO Bioorganic & Medicinal Chemistry (2002), 10(6), 1659-1670  
 CODEN: BMECEP; ISSN: 0968-0896  
 PB Elsevier Science Ltd.  
 DT Journal  
 LA English  
 OS CASREACT 137:60114  
 IT **439152-40-6P**  
 RL: BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (new synthetic siderophores and their .beta.-lactam conjugates based on diamino acids and dipeptides)  
 RN 439152-40-6 CAPLUS  
 CN Glycinamide, N2,N5-bis[2,3-bis(acetyloxy)benzoyl]-L-ornithyl-L-phenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Linking of siderophores to antibiotics improves the penetration and therefore increases the antibacterial activity of the antibiotics. We synthesized the acylated catecholates and hydroxamates as siderophore components for antibiotic conjugates to reduce side effects of unprotected catecholate and hydroxamate moieties. In this paper, we report on bis- and tris-catecholates and mixed catecholate hydroxamates based on diamino acids or dipeptides. These compds. were active as siderophores in a growth promotion assay under Fe limitation. Most of the conjugates with .beta.-lactams showed high in vitro activity against Gram-neg. bacteria, esp. *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Serratia marcescens*, and *Stenotrophomonas maltophilia*. The compds. with enhanced antibacterial activity use active Fe uptake routes to penetrate the bacterial outer membrane barrier, demonstrated by assays with mutants

deficient in components of the Fe transport system. Correlation between chem. structure and biol. activity was studied.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 2002:157723 CAPLUS

DN 136:216523

TI Preparation of phenylethanol(mono/di)amines and  
phenylalkylethanol(mono/di)amines as sodium channel blockers

IN Fuchs, Klaus; Stransky, Werner; Grauert, Matthias; Carter, Adrian; Gaida, Wolfram; Weiser, Thomas; Ensinger, Helmut

PA Boehringer Ingelheim Pharma K.-G., Germany

SO PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

|    | PATENT NO.    | KIND | DATE     | APPLICATION NO.   | DATE   |
|----|---------------|------|----------|-------------------|--|
| PI | WO 2002016308 | A1   | 20020228 | WO 2001-EP9036    | 20010804   |
|    | W:            |      |          |                   |  |
|    |               |      |          |                   | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |
|    | RW:           |      |          |                   | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |
|    | DE 10040901   | A1   | 20020314 | DE 2000-10040901A | 20000818   |
|    | US 2002042410 | A1   | 20020411 | US 2001-912163    | 20010724   |
|    |               |      |          | DE 2000-10040901A | 20000818   |
|    |               |      |          | US 2000-228675PP  | 20000829   |
| AU | 2001091737    | A5   | 20020304 | AU 2001-91737     | 20010804   |
|    |               |      |          | DE 2000-10040901A | 20000818   |
|    |               |      |          | WO 2001-EP9036 W  | 20010804   |
| EP | 1311471       | A1   | 20030521 | EP 2001-971870    | 20010804   |
|    | R:            |      |          |                   | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |
|    |               |      |          | DE 2000-10040901A | 20000818   |
|    |               |      |          | WO 2001-EP9036 W  | 20010804   |

CS MARPAT 136:216523

IT 401938-19-0P 401938-31-6P 401938-36-1P  
401938-38-3P 401938-45-2P 401938-49-6P  
401938-53-2P 401938-55-4P 401938-57-6P  
401938-61-2P 401938-63-4P 401938-69-0P  
401938-73-6P 401938-75-8P 401938-77-0P  
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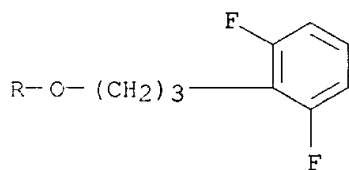
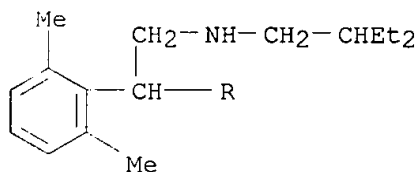
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of phenylethanolamines and phenylalkylethanolamines as sodium channel blockers)

RN 401938-19-0 CAPLUS

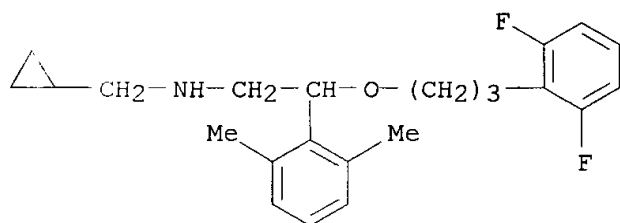


CN Benzeethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-N-(2-ethylbutyl)-  
2,6-dimethyl- (9CI) (CA INDEX NAME)



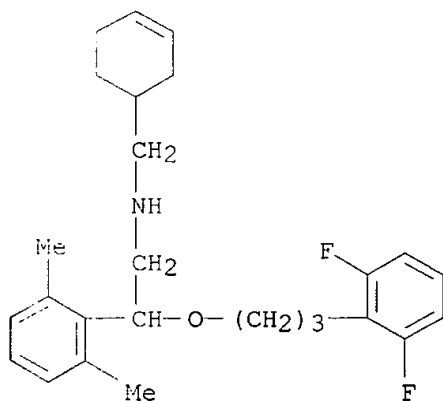
RN 401938-31-6 CAPLUS

CN Benzeethanamine, N-(cyclopropylmethyl)-.beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl- (9CI) (CA INDEX NAME)



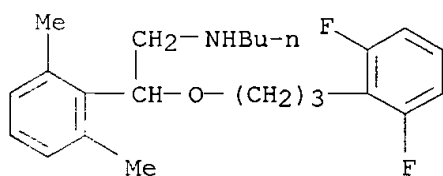
RN 401938-36-1 CAPLUS

CN Benzeethanamine, N-(3-cyclohexen-1-ylmethyl)-.beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl- (9CI) (CA INDEX NAME)



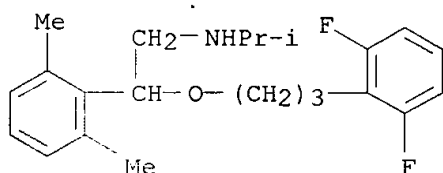
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CN Benzeneethanamine, N-butyl-.beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl- (9CI) (CA INDEX NAME)



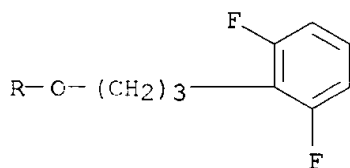
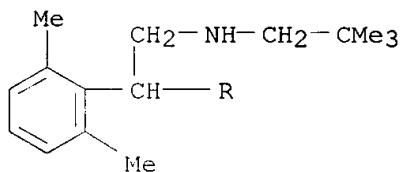
RN 401938-45-2 CAPLUS

CN Benzeethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



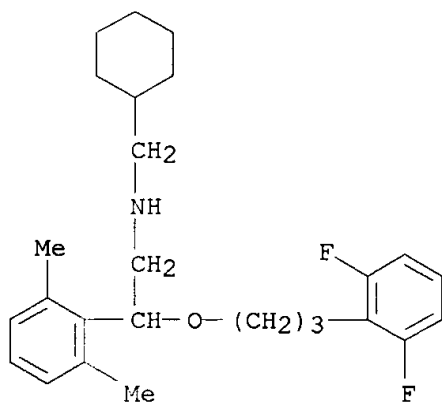
RN 401938-49-6 CAPLUS

CN Benzeethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-N-(2,2-dimethylpropyl)-2,6-dimethyl- (9CI) (CA INDEX NAME)



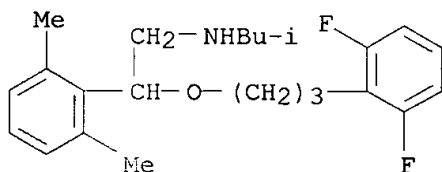
RN 401938-53-2 CAPLUS

CN Benzeethanamine, N-(cyclohexylmethyl)-.beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl- (9CI) (CA INDEX NAME)



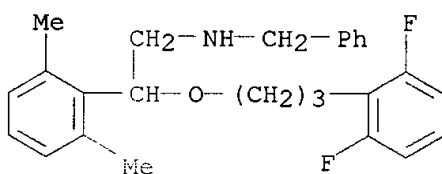
RN 401938-55-4 CAPLUS

CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-(2-methylpropyl)- (9CI) (CA INDEX NAME)



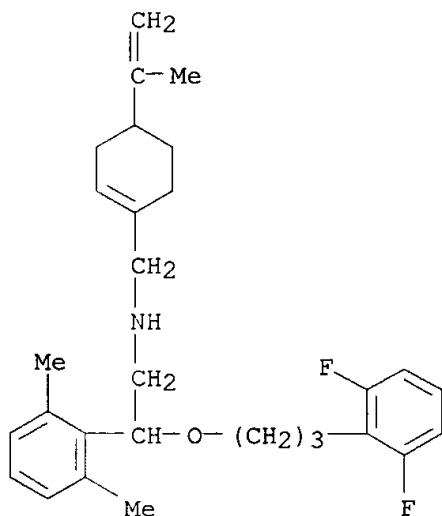
RN 401938-57-6 CAPLUS

CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



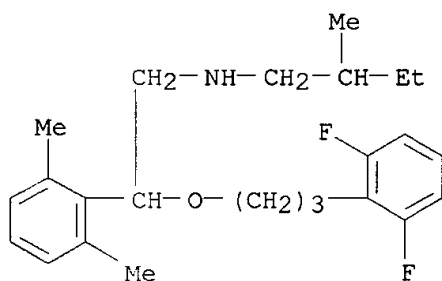
RN 401938-61-2 CAPLUS

CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-[[4-(1-methylethenyl)-1-cyclohexen-1-yl]methyl]- (9CI) (CA INDEX NAME)



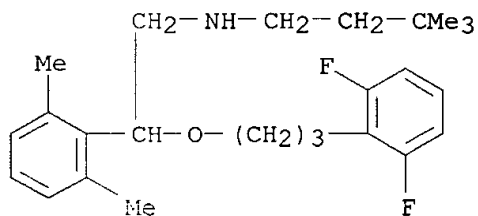
RN 401938-63-4 CAPLUS

CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-(2-methylbutyl)- (9CI) (CA INDEX NAME)



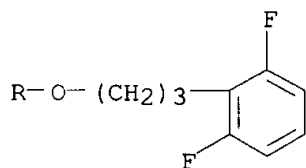
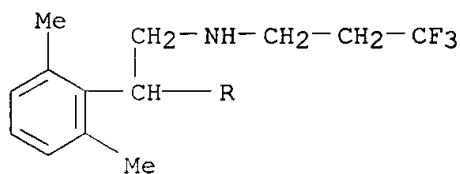
RN 401938-69-0 CAPLUS

CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-N-(3,3-dimethylbutyl)-2,6-dimethyl- (9CI) (CA INDEX NAME)



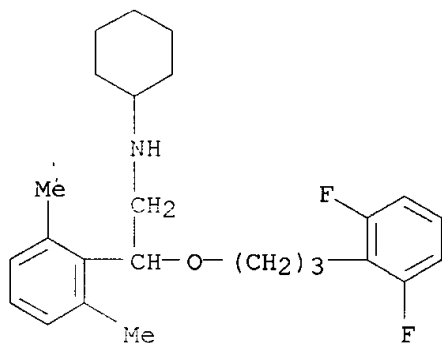
RN 401938-73-6 CAPLUS

CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-(3,3,3-trifluoropropyl)- (9CI) (CA INDEX NAME)



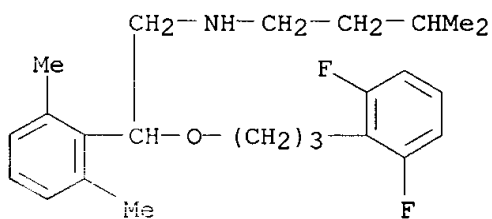
RN 401938-75-8 CAPLUS

CN Benzeneethanamine, N-cyclohexyl-.beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl- (9CI) (CA INDEX NAME)



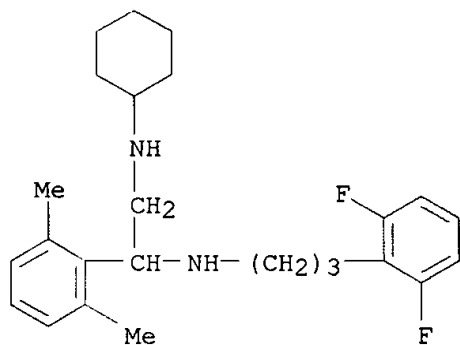
RN 401938-77-0 CAPLUS

CN Benzeneethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-(3-methylbutyl)- (9CI) (CA INDEX NAME)



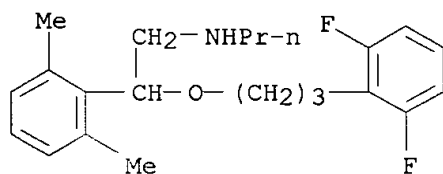
RN 401939-43-3 CAPLUS

CN 1,2-Ethanediamine, N2-cyclohexyl-N1-[3-(2,6-difluorophenyl)propyl]-1-(2,6-dimethylphenyl)- (9CI) (CA INDEX NAME)



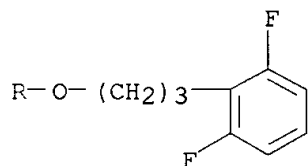
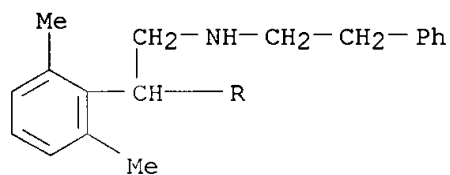
RN 401939-56-8 CAPLUS

CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-propyl- (9CI) (CA INDEX NAME)



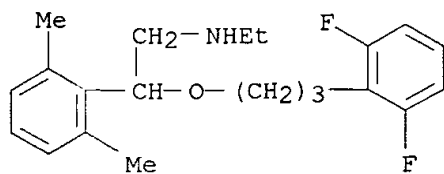
RN 401939-58-0 CAPLUS

CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-(2-phenylethyl)- (9CI) (CA INDEX NAME)



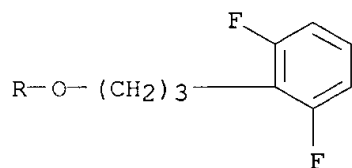
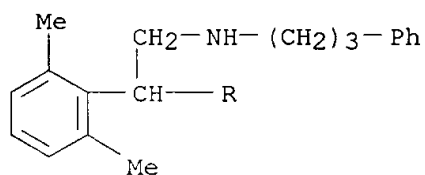
RN 401939-80-8 CAPLUS

CN Benzenethanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-N-ethyl-2,6-dimethyl- (9CI) (CA INDEX NAME)



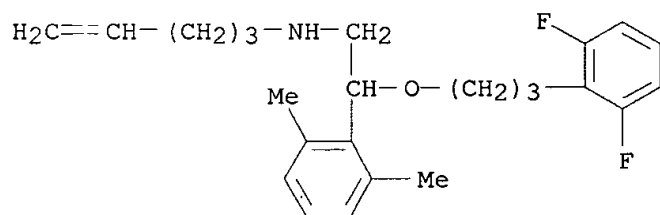
RN 401939-82-0 CAPLUS

CN Benzenepropanamine, N-[2-[3-(2,6-difluorophenyl)propoxy]-2-(2,6-dimethylphenyl)ethyl]- (9CI) (CA INDEX NAME)

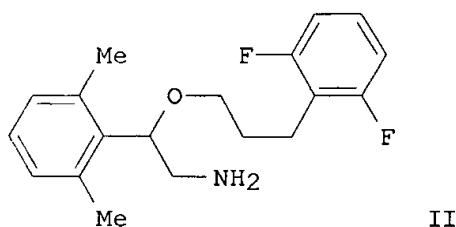
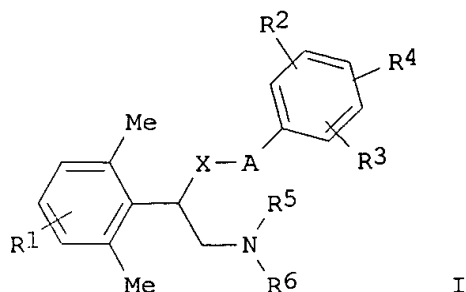


RN 401939-84-2 CAPLUS

CN Benzenepropanamine, .beta.-[3-(2,6-difluorophenyl)propoxy]-2,6-dimethyl-N-4-pentenyl- (9CI) (CA INDEX NAME)



GI



AB Title compds. [I; R1 = OH, CF3, NO2, CN, halo, C1-8 alkyl, halo, C1-8 alkoxy; R2, R3, R4 independently = halo, C1-8 alkyl, OH, NO2, CN, C1-8 alkoxy, CF3; R5, R6 independently = C1-8 alkyl, C2-8 alkenyl, C3-8 alkynyl, C3-8 cycloalkyl, NH2, OH, O, COOH, CONH2; A = C1-5 alkylene, C2-4 alkenylene, C3-4 alkylene; X = NH, N(CHO), halo, O, etc.] are prepd. The invention further relates to a method for producing said compds. and to their compn. in use as medicaments. Title compds. I are used as blockers of the voltage-dependent sodium channel and can be used for diseases that are assocd. with a functional disorder caused by hyperexcitability. Thus, the title compd. II was prepd. from trifluoroacetic anhydride, 2,6-dimethylbenzaldehyde, which was prepd. from 2-bromo-3-dimethylbenzene, and 2-(3-bromopropyl)-1,3-difluorobenzene, which was prepd. from di-Et malonate and 2,6-difluorobenzyl bromide.

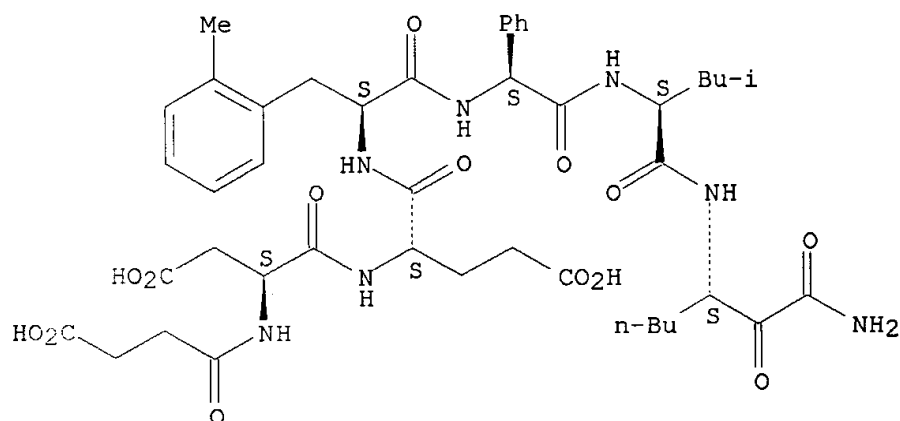
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 148 CAPLUS COPYRIGHT 2003 ACS  
AN 2002:116966 CAPLUS  
DN 137:125377  
TI Solution and solid-Phase synthesis of potent inhibitors of hepatitis C Virus NS3 proteinase  
AU Beevers, Rebekah; Carr, Maria G.; Jones, Philip S.; Jordan, Steven; Kay, Paul B.; Lazell, Robert C.; Raynham, Tony M.  
CS Department of Chemistry, Roche Discovery Welwyn, Hertfordshire, Welwyn Garden City, AL7 3AY, UK  
SO Bioorganic & Medicinal Chemistry Letters (2002), 12(4), 641-643  
CODEN: BMCLE8; ISSN: 0960-894X  
PB Elsevier Science Ltd.  
DT Journal



LA English  
 OS CASREACT 137:125377  
 IT 254439-10-6P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (prepn. and biol. activity of peptide .alpha.-ketoamides as potent inhibitors of hepatitis C virus NS3 proteinase)  
 RN 254439-10-6 CAPLUS  
 CN L-Leucinamide, N-(3-carboxy-1-oxopropyl)-L-.alpha.-aspartyl-L-.alpha.-glutamyl-2-methyl-L-phenylalanyl-(2S)-2-phenylglycyl-N-[(1S)-1-(aminooxoacetyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB A versatile route for the synthesis of homochiral .alpha.-ketoamide analogs of amino acids is described. Incorporation of this functionality into peptide sequences using either soln. or solid-phase chem. resulted in potent inhibitors of the hepatitis C virus (HCV) NS3 proteinase.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 2002:31402 CAPLUS  
 DN 136:102190  
 TI Preparation of substituted amines to treat Alzheimer's disease  
 IN Maillaird, Michel; Hom, Court; Gailunas, Andrea; Jagodzinska, Barbara; Fang, Lawrence Y.; John, Varghese; Freskos, John N.; Pulley, Shon R.; Beck, James P.; Tenbrink, Ruth E.  
 PA Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company  
 SO PCT Int. Appl., 651 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 5

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2002002512   | A2   | 20020110 | WO 2001-US21012 | 20010629 |
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 US 2000-255956PP 20001215  
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 US 2001-896139 20010629  
 US 2000-215323PP 20000630  
 US 2000-252736PP 20001122  
 US 2000-255956PP 20001215  
 US 2001-268497PP 20010213  
 US 2001-279779PP 20010329  
 US 2001-295589PP 20010604  
 NO 2002-6199 20021223  
 US 2000-215323PP 20000630  
 US 2000-252736PP 20001122  
 US 2000-255956PP 20001215  
 US 2001-268497PP 20010213  
 US 2001-279779PP 20010329  
 US 2001-295589PP 20010604  
 WO 2001-US21012W 20010629

## PATENT FAMILY INFORMATION:

FAN 2002:31396

|               | PATENT NO.   | KIND     | DATE           | APPLICATION NO.  | DATE     |
|---------------|--|----------|----------------|------------------|----------|
| PI            | WO 2002002505  | A2       | 20020110       | WO 2001-US20852  | 20010629 |
|               | WO 2002002505  | A3       | 20020801       |                  |          |
| W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                |                  |          |
| RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |          |                |                  |          |
|               | US 2002016320  | A1       | 20020207       | US 2000-215323PP | 20000630 |
|               |  |          |                | US 2001-896874   | 20010629 |
|               |  |          |                | US 2000-215323PP | 20000630 |
| EP 1299349    | A2   | 20030409 | EP 2001-950719 | 20010629         |          |
| R:            | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |          |                |                  |          |
|               |  |          |                | US 2000-215323PP | 20000630 |
|               |  |          |                | WO 2001-US20852W | 20010629 |
| US 2003096864 | A1   | 20030522 | US 2001-895871 | 20010629         |          |
|               |  |          |                | US 2000-215323PP | 20000630 |

FAN 2002:31397

|  | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------------|------|------|-----------------|------|
|  |            |      |      |                 |      |

|     |               |  |          |                  |          |
|-----|---------------|--|----------|------------------|----------|
| PI  | WO 2002002506 | A2   | 20020110 | WO 2001-US20930  | 20010629 |
|     | W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                  |          |
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|     | US 2002016320 | A1   | 20020207 | US 2000-215323PP | 20000630 |
|     |               |  |          | US 2001-896874   | 20010629 |
|     |               |  |          | US 2000-215323PP | 20000630 |
|     | EP 1299352    | A2   | 20030409 | EP 2001-952352   | 20010629 |
|     | R:            | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |          |                  |          |
|     |               |  |          | US 2000-215323PP | 20000630 |
|     |               |  |          | WO 2001-US20930W | 20010629 |
|     | US 2003096864 | A1   | 20030522 | US 2001-895871   | 20010629 |
|     |               |  |          | US 2000-215323PP | 20000630 |
| FAN | 2002:31408    |  |          |                  |          |
|     | PATENT NO.    | KIND   | DATE     | APPLICATION NO.  | DATE     |
| PI  | WO 2002002518 | A2   | 20020110 | WO 2001-US20856  | 20010629 |
|     | WO 2002002518 | A3   | 20020808 |                  |          |
|     | W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                  |          |
|     | RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |          |                  |          |
|     |               |  |          | US 2000-215323PP | 20000630 |
|     | AU 2001073094 | A5   | 20020114 | AU 2001-73094    | 20010629 |
|     |               |  |          | US 2000-215323PP | 20000630 |
|     |               |  |          | WO 2001-US20856W | 20010629 |
|     | US 2002016320 | A1   | 20020207 | US 2001-896874   | 20010629 |
|     |               |  |          | US 2000-215323PP | 20000630 |
|     | US 2003096864 | A1   | 20030522 | US 2001-895871   | 20010629 |
|     |               |  |          | US 2000-215323PP | 20000630 |
| FAN | 2002:31410    |  |          |                  |          |
|     | PATENT NO.    | KIND   | DATE     | APPLICATION NO.  | DATE     |
| PI  | WO 2002002520 | A2   | 20020110 | WO 2001-US21000  | 20010702 |
|     | W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                  |          |
|     | RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |          |                  |          |

US 2002143177 A1 20021003  
 AU 2001073132 A5 20020114

US 2000-215323PP 20000630  
 US 2001-895843 A 20010629  
 US 2001-895843 20010629  
 US 2000-215323PP 20000630  
 AU 2001-73132 20010702  
 US 2000-215323PP 20000630  
 US 2001-895843 A 20010629  
 WO 2001-US21000W 20010702

OS MARPAT 136:102190

IT **388063-36-3P**

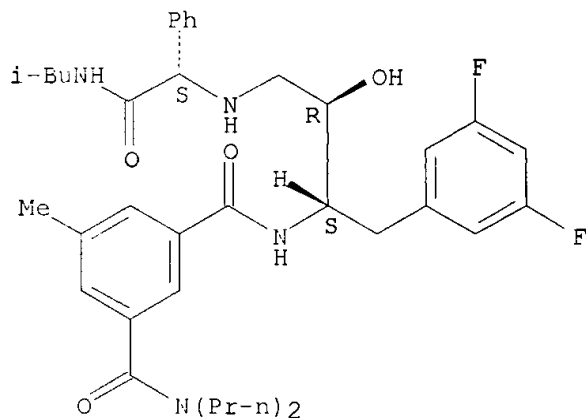
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(prepn. of substituted amines for treating Alzheimer's disease)

RN 388063-36-3 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[[(1S)-2-[(2-methylpropyl)amino]-2-oxo-1-phenylethyl]amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **388073-92-5 388075-22-7**

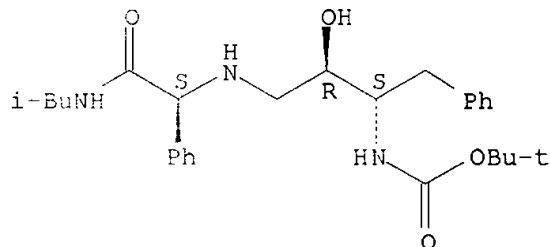
RL: RCT (Reactant); RACT (Reactant or reagent)

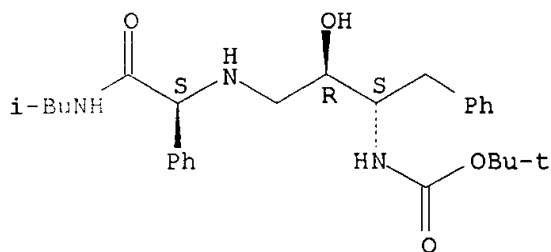
(prepn. of substituted amines for treating Alzheimer's disease)

RN 388073-92-5 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[[[(1S)-2-[(2-methylpropyl)amino]-2-oxo-1-phenylethyl]amino]-1-(phenylmethyl)propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

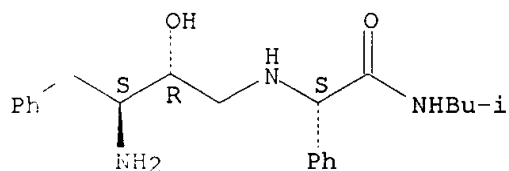




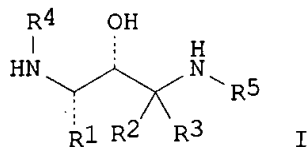
RN 388075-22-7 CAPLUS

CN Benzeneacetamide, .alpha.-[[(2R,3S)-3-amino-2-hydroxy-4-phenylbutyl]amino]-N-(2-methylpropyl)-, (.alpha.S)- (9CI) (CA INDEX NAME)

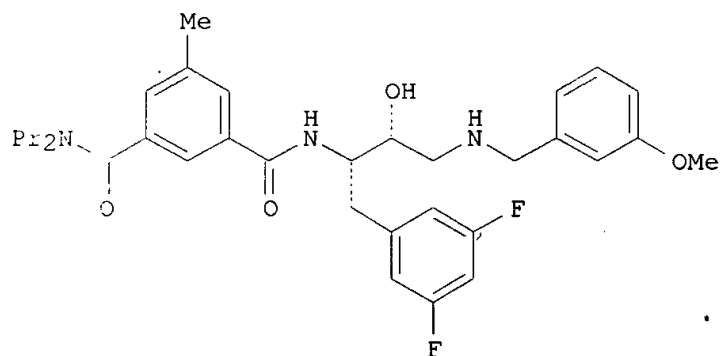
Absolute stereochemistry.



GI



I



II

AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO2, a bond, etc.; R = Ph,

naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH<sub>2</sub>)<sub>0-3</sub>cycloalkyl, etc.], useful in treating Alzheimer's disease and other similar diseases, were prepd. Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthalamide in the presence of Et<sub>3</sub>N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II. The compds. I exhibit an IC<sub>50</sub> of < 50 .mu.M against beta-secretase.

L4 ANSWER 11 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 2001:851126 CAPLUS

DN 135:371760

TI Preparation of pyrazolylpyrimidines and analogs as TNF-.alpha. signaling modulators

IN Sneddon, Scott F.; Kane, John L.; Hirth, Bradford H.; Vinick, Fred; Qiao, Shuang; Nahill, Sharon R.

PA Genzyme Corporation, USA

SO PCT Int. Appl., 108 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO.  | DATE     |
|----|--|------|----------|------------------|----------|
| PI | WO 2001087849  | A2   | 20011122 | WO 2001-US15027  | 20010510 |
|    | WO 2001087849  | A3   | 20020606 |                  |          |
|    | W:   |      |          |                  |          |
|    | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                  |          |
|    | RW:  |      |          |                  |          |
|    | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |      |          |                  |          |
|    |  |      |          | US 2000-203784PP | 20000512 |
|    |  |      |          | US 2000-205213PP | 20000518 |
|    | US 2002119988  | A1   | 20020829 | US 2001-852965   | 20010510 |
|    |  |      |          | US 2000-203784PP | 20000512 |
|    |  |      |          | US 2000-205213PP | 20000518 |
|    | EP 1294699   | A2   | 20030326 | EP 2001-933253   | 20010510 |
|    | R:   |      |          |                  |          |
|    | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |      |          |                  |          |
|    |  |      |          | US 2000-203784PP | 20000512 |
|    |  |      |          | US 2000-205213PP | 20000518 |
|    |  |      |          | WO 2001-US15027W | 20010510 |
|    | NO 2002005405  | A    | 20030109 | NO 2002-5405     | 20021111 |
|    |  |      |          | US 2000-203784PP | 20000512 |
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|    |  |      |          | WO 2001-US15027W | 20010510 |

OS HARPAT 135:371760

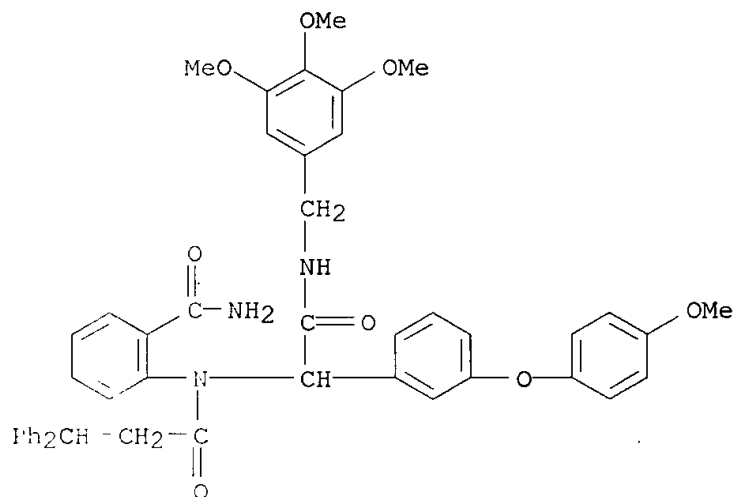
IT 374080-34-9P 374080-37-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of pyrazolylpyrimidines and analogs as TNF-.alpha. signaling modulators)

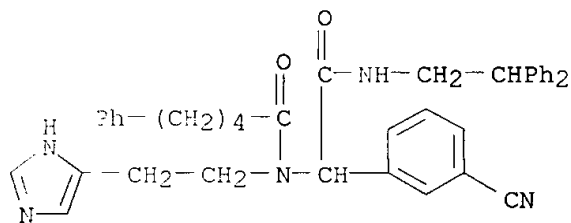
PN 374080-34-9 CAPLUS

CN Benzenepropanamide, N-[2-(aminocarbonyl)phenyl]-N-[1-[3-(4-methoxyphenoxy)phenyl]-2-oxo-2-[[ (3,4,5-trimethoxyphenyl)methyl]amino]ethyl]-.beta.-phenyl- (9CI) (CA INDEX NAME)

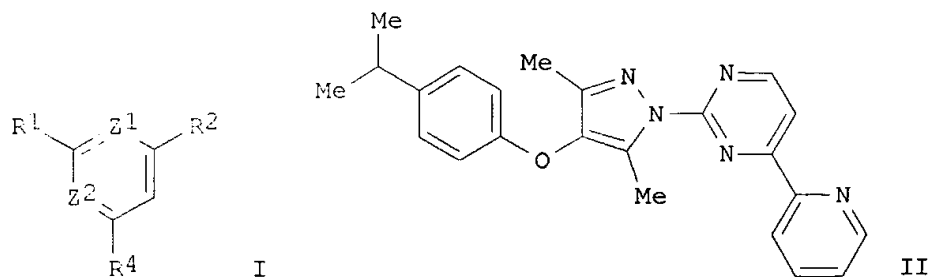


RN 374080-37-2 CAPLUS

CN Benzenepentanamide, N-[1-(3-cyanophenyl)-2-[(2,2-diphenylethyl)amino]-2-oxoethyl]-N-[2-(1H-imidazol-4-yl)ethyl]- (9CI) (CA INDEX NAME)



GI



AB Title compds. [I; R1 = H or NH2; R2 = ZZ3(CH2)nR; R = (un)substituted Ph

or -heterocyclyl; R4 = (alkyl-substituted) 2-pyridinyl or -pyrazinyl; Z = (un)substituted pyrazole-1,4-diyl; Z1,Z2 = N or CH; Z3 = O, CH2, S, SO2; n = 0-2] were prep'd. Thus, 4-(Me2HC)C6H4OH was condensed with (MeCO)2CHN2 and the product cyclocondensed with 4-(2-pyridinyl)-2-pyrimidinylhydrazine to give title comp'd. II. Data for biol. activity of I were given.

L4 ANSWER 12 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 2001:818819 CAPLUS

DN 136:118732

TI A Rapid Access to Biaryl Ether Containing Macrocycles by Pairwise Use of Ugi 4CR and Intramolecular SNAr-Based Cycloetherification

AU Cristau, Pierre; Vors, Jean-Pierre; Zhu, Jieping

CS Institut de Chimie des Substances Naturelles, CNRS, Gif-sur-Yvette, 91198, Fr.

SO Organic Letters (2001), 3(25), 4079-4082

CODEN: ORLEF7; ISSN: 1523-7060

PB American Chemical Society

DT Journal

LA English

OS CASREACT 136:118732

IT 389634-87-1P 389634-98-4P

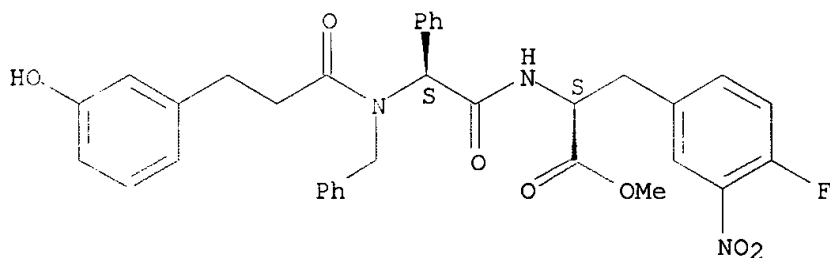
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of biaryl ether-contg. macrocycles by Ugi four component reaction and intramol. SNAr-based cycloetherification)

RN 389634-87-1 CAPLUS

CN D-Phenylalanine, (2R)-N-[3-(3-hydroxyphenyl)-1-oxopropyl]-2-phenyl-N-(phenylmethyl)glycyl-4-fluoro-3-nitro-, methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

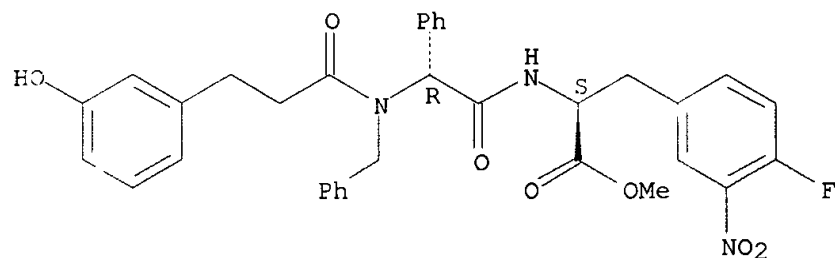


RN 389634-98-4 CAPLUS

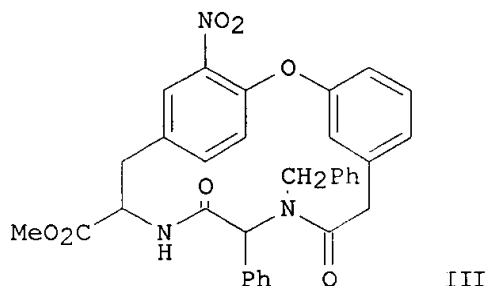
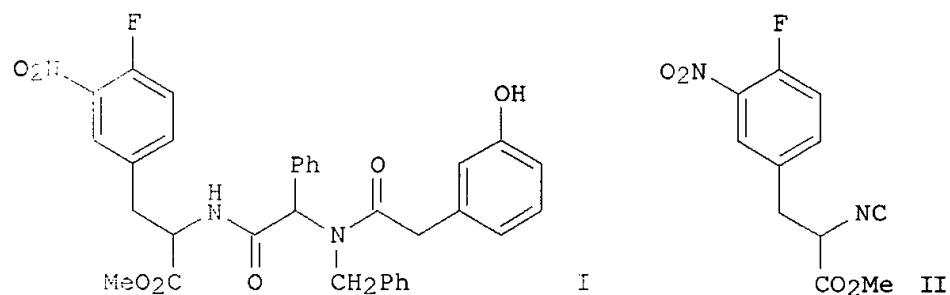
CN D-Phenylalanine, (2S)-N-[3-(3-hydroxyphenyl)-1-oxopropyl]-2-phenyl-N-(phenylmethyl)glycyl-4-fluoro-3-nitro-, methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.





GI



AB An Ugi reaction promoted by ammonium chloride in aprotic solvent is documented here for the first time. From readily accessible starting materials, macrocycles with an endo aryl-aryl ether bond are synthesized in only two steps, Ugi four-component reaction (Ugi 4CR) and an intramol. SNAr reaction. The nitro group serves as an activator for the macrocyclization and provides a handle for the introduction of functional group diversity. For example, dipeptide amide I was obtained in an Ugi 4CR from isonitrile II, PhCHO, PhCH<sub>2</sub>NH<sub>2</sub> and 3-hydroxyphenylacetic acid in the presence of NH<sub>4</sub>Cl- in toluene at 0.degree. for 20 h. Cycloetherification of I took place in the presence of K<sub>2</sub>CO<sub>3</sub> in DMF for 3 h to give macrocycle III in 80% yield.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 148 CAPLUS COPYRIGHT 2003 ACS  
AN 2001:631914 CAPLUS  
DI 135:195426

TI Preparation of malonic acid amide derivatives as inhibitors of blood clotting factor Xa

IN Al-Obeidi, Fahad; Walser, Armin; Wildgoose, Peter

PA Aventis Pharma Deutschland G.m.b.H., Germany

SO Eur. Pat. Appl., 69 pp.

CODEN: EPXXDW

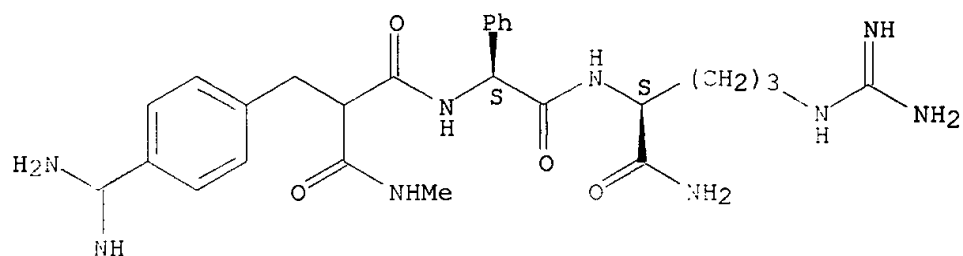
DT Patent

LA English

FAN.CNT 1

|     | PATENT NO.  | KIND | DATE     | APPLICATION NO.  | DATE     |
|-----|---|------|----------|------------------|----------|
| PI  | EP 1127884  | A1   | 20010829 | EP 2000-104041   | 20000226 |
|     | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |      |          |                  |          |
|     | BR 2001008694   | A    | 20021210 | BR 2001-8694     | 20010121 |
|     |   |      |          | EP 2000-104041 A | 20000226 |
|     |   |      |          | WO 2001-EP1928 W | 20010221 |
|     | WO 2001062735   | A1   | 20010830 | WO 2001-EP1928   | 20010221 |
|     | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                  |          |
|     | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                  |          |
|     |   |      |          | EP 2000-104041 A | 20000226 |
|     | EP 1265867  | A1   | 20021218 | EP 2001-907546   | 20010221 |
|     | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |      |          |                  |          |
|     |   |      |          | EP 2000-104041 A | 20000226 |
|     |   |      |          | WO 2001-EP1928 W | 20010221 |
|     | US 2002022596   | A1   | 20020221 | US 2001-790641   | 20010223 |
|     |   |      |          | EP 2000-104041 A | 20000226 |
|     | NO 200204040  | A    | 20020924 | NO 2002-4040     | 20020823 |
|     |   |      |          | EP 2000-104041 A | 20000226 |
|     |   |      |          | WO 2001-EP1928 W | 20010221 |
| OS  | MARPAT 135:195426   |      |          |                  |          |
| IT  | 356544-17-7P 356544-20-2P 356544-22-4P 356544-24-6P   |      |          |                  |          |
|     | RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)   |      |          |                  |          |
|     | (drug; prepn. of malonic acid amide derivs. as inhibitors of blood clotting factor Xa)  |      |          |                  |          |
| RN  | 356544-17-7 CAPLUS  |      |          |                  |          |
| CN  | L-Argininamide, 2-[[4-(aminoiminomethyl)phenyl]methyl]-N-methyl-3-oxo-.beta.-alanyl-(2S)-2-phenylglycyl-, trifluoroacetate (9CI) (CA INDEX NAME)  |      |          |                  |          |
| CM  | 1   |      |          |                  |          |
| CRN | 356544-16-6   |      |          |                  |          |
| CMF | C26 H35 N9 O4   |      |          |                  |          |

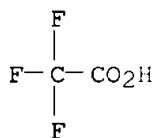
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 356544-20-2 CAPLUS

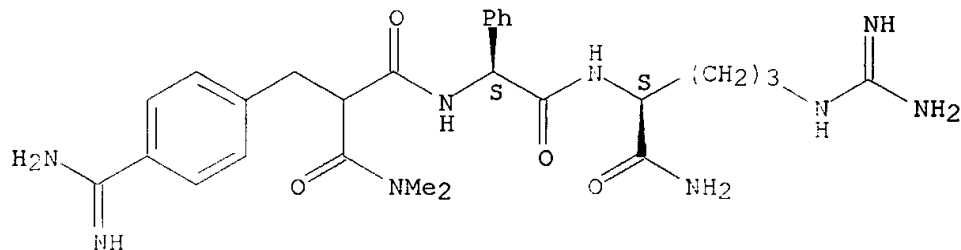
CH L-Argininamide, 2-[[4-(aminoiminomethyl)phenyl]methyl]-N,N-dimethyl-3-oxo-  
 .beta.-alanyl-(2S)-2-phenylglycyl-, trifluoroacetate (9CI) (CA INDEX  
 NAME)

CM 1

CRN 356544-19-9

CMF C27 H37 N9 O4

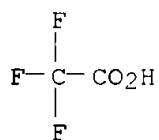
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 356544-22-4 CAPLUS

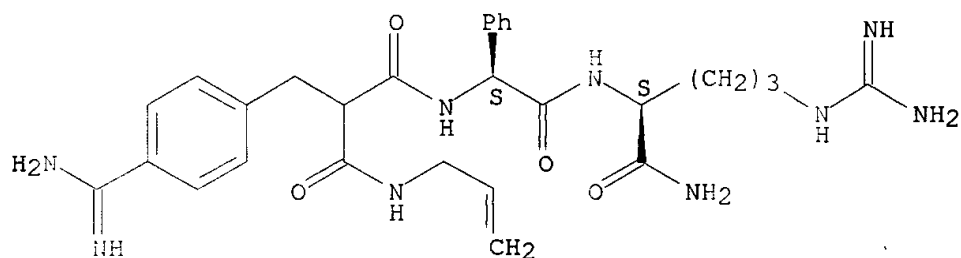
CN L-Argininamide, 2-[[4-(aminoiminomethyl)phenyl]methyl]-3-oxo-N-2-propenyl-.beta.-alanyl-(2S)-2-phenylglycyl-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 356544-21-3

CMF C28 H37 N9 O4

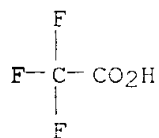
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 356544-24-6 CAPLUS

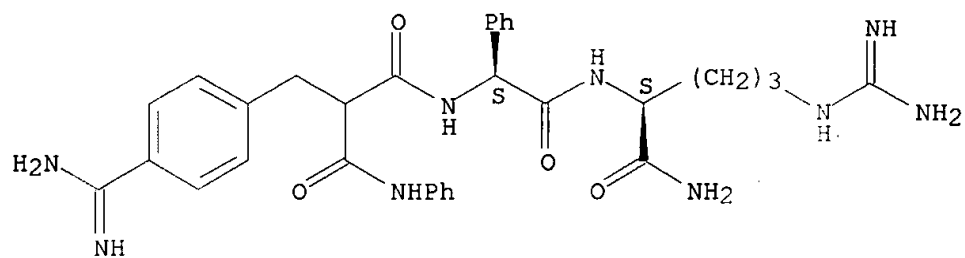
CN L-Argininamide, 2-[[4-(aminoiminomethyl)phenyl]methyl]-3-oxo-N-phenyl-.beta.-alanyl-(2S)-2-phenylglycyl-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 356544-23-5

CMF C31 H37 N9 O4

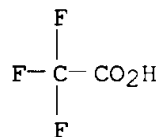
Absolute stereochemistry.



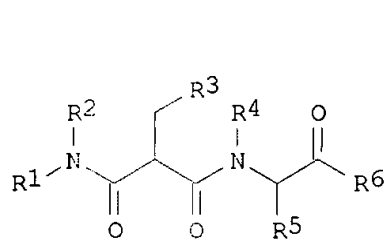
CM 2

CRN 76-05-1

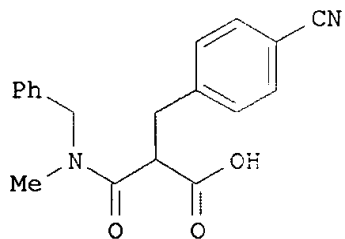
CMF C2 H F3 O2



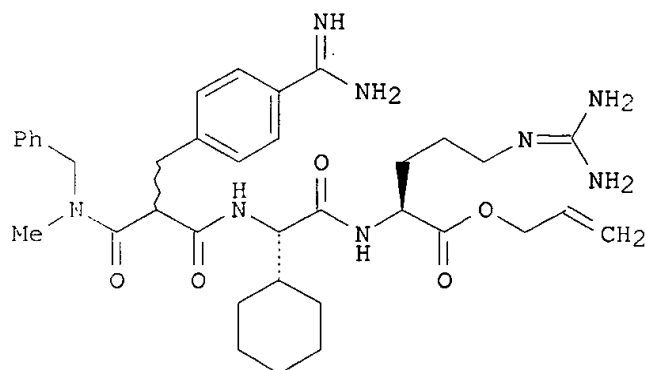
GI



I



II



III

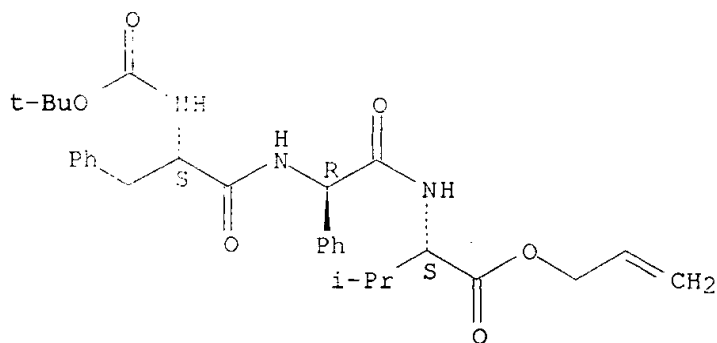
AB Title compds. I [ $\text{R}_1$  = H, alk(en)yl, aryl(alkyl);  $\text{R}_2$  = H, alkyl;  $\text{R}_3$  = aryl;

R4 = H, alkyl, etc.; R5 = (cyclo)alkyl, cycloalkyl-alkyl, aryl(alkyl), etc.; R6 = NH<sub>2</sub>, OH or substituted derivs.] are prepd. Examples included 3 synthetic procedures (including a general solid phase method), over 100 compds. prepd. and 8 bioassays (data provided for 1 of the bioassays). For instance, benzyl Me amine was treated with bis(trimethylsilyl)acetamide (DCM, reflux, 3 h) followed by addn. of 4-[(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)methyl]benzonitrile (DCM, reflux, 3 h) to give II. II was coupled to (.alpha.S)-amino-cyclohexane-acetic acid Me ester (iPr<sub>2</sub>EtN, HODhbt, DCC, DMF, 10.degree.C) and the resulting amide-nitrile reacted with excess hydroxylamine (EtOH, reflux, 4 h) to give the corresponding N-hydroxy carbamimidoyl deriv. This intermediate was deoxygenated (Pd-H<sub>2</sub>/C), hydrolyzed (HCl aq, CH<sub>3</sub>CN, 4 days @ room temp.) and coupled with (S)-2-amino-5-guanidinopentanoic acid allyl ester (DMF, collidine, HATU) to give III. Isomers of III were sepd. by chromatog. (MPLC, RP18) and isolated as the trifluoroacetic acid salts. An isomer of III had K<sub>i</sub> = 0.0010 .mu.M for factor Xa. The invention also provides methods for the treatment/prevention of (e.g.) thromboembolic diseases.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 148 CAPLUS COPYRIGHT 2003 ACS  
AN 2001:557633 CAPLUS  
DN 135:344705  
TI A new silyl linker for reverse-direction solid-phase peptide synthesis  
AU Lipshutz, B. H.; Shin, Y.-J.  
CS Department of Chemistry & Biochemistry, University of California, Santa Barbara, CA, 93106, USA  
SO Tetrahedron Letters (2001), 42(33), 5629-5633  
CODEN: TELEAY; ISSN: 0040-4039  
PB Elsevier Science Ltd.  
DT Journal  
LA English  
IT 370866-93-6P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(reverse-direction solid-phase peptide synthesis using  
(chloro)diisopropylsilyl-linked polystyrene)  
RN 370866-93-6 CAPLUS  
CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-(2R)-2-phenylglycyl-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

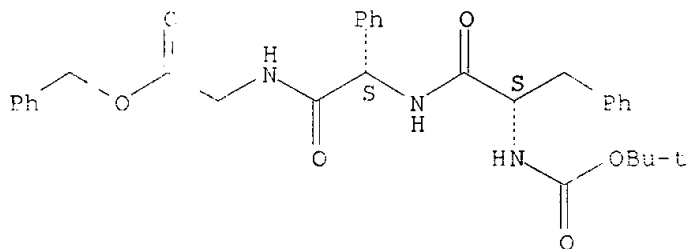


AB Treatment of a free amino acid ester with carbon dioxide followed by exposure to a chlorosilane-contg. polystyrene results in its attachment to the solid support. For example, H-Pro-OAll (All = allyl) was coupled with CO<sub>2</sub> in Et<sub>3</sub>N, followed by the addn. of ClSi(Pr-i)<sub>2</sub>-polystyrene, to give 95% of polystyrene-Si(Pr-i)<sub>2</sub>O<sub>2</sub>C-Pro-OAll (I). The newly formed silyl carbamate can be employed to build polypeptides at the carboxyl terminus. Cleavage of the (poly)peptide using aq. HF in MeCN leads to its free amine form which is isolated as a Boc deriv. Thus, I was utilized in peptide synthesis and Boc-protected in the last step to give Boc-Pro-D-Phg-Phe-OAll (D-Phg = D-phenylglycyl) in 52% overall yield. The polymer support can be easily recycled.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

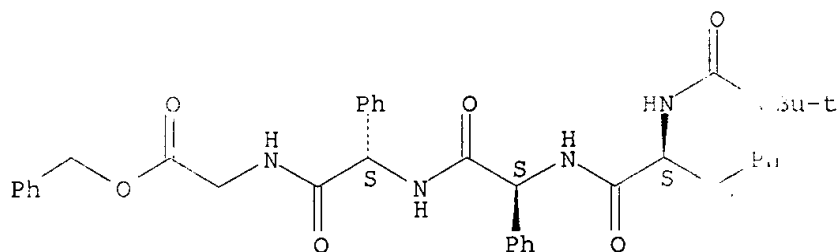
L4 ANSWER 15 OF 148 CAPLUS COPYRIGHT 2003 ACS  
AN 2001:4:0630 CAPLUS  
DN 136:2:0452  
TI Synthesis of a number of combined analogs of substance P and litorin  
AU Galyuk, E. N.; Egorova, S. V.; Gurina, E. P.; Golubovich, V. P.; Akhrem, A. A.  
CS Inst. Bioorganic Chem., Belorussian Acad. Sci., Minsk, Russia  
SO Khimiya Prirodnikh Soedinenii (1992), (1), 112-117  
CODEN:KPSUAR; ISSN: 0023-1150  
PB Izdatel'stvo Fan  
DT Journal  
LA Russian  
IT 400748-27-8P 400748-33-6P 400748-68-7P  
400749-12-4P 400749-61-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of substance P and litorin analogs by peptide coupling)  
RN 400748-27-8 CAPLUS  
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-(2S)-2-phenylglycyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 400748-33-6 CAPLUS  
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-(2S)-2-phenylglycyl-(2S)-2-phenylglycyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

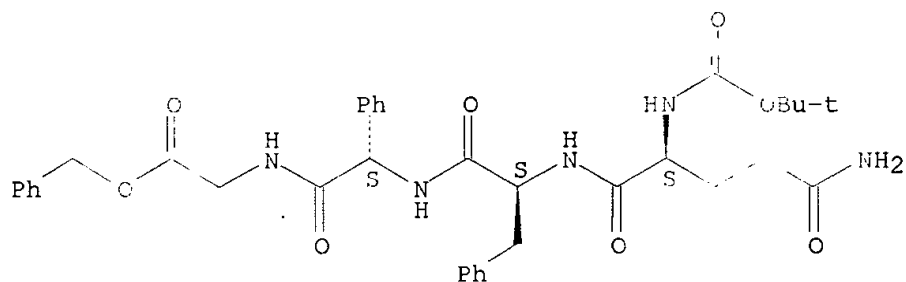
Absolute stereochemistry. Rotation (+).



RN 400748-68-7 CAPLUS

CN Glycine, N2-[(1,1-dimethylethoxy)carbonyl]-L-glutaminy-L-phenylalanyl-(2S)-2-phenylglycyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

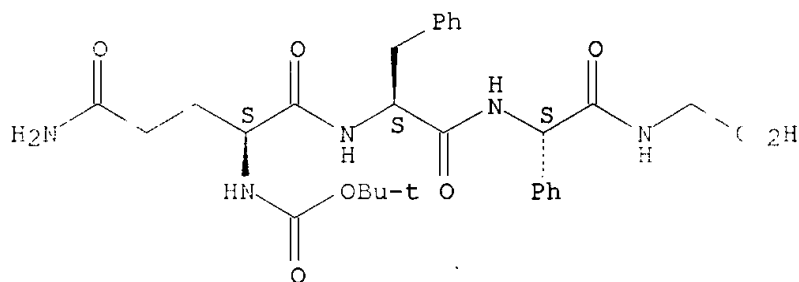
Absolute stereochemistry. Rotation (+).



RN 400749-12-4 CAPLUS

CN Glycine, N2-[(1,1-dimethylethoxy)carbonyl]-L-glutaminy-L-phenylalanyl-(2S)-2-phenylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

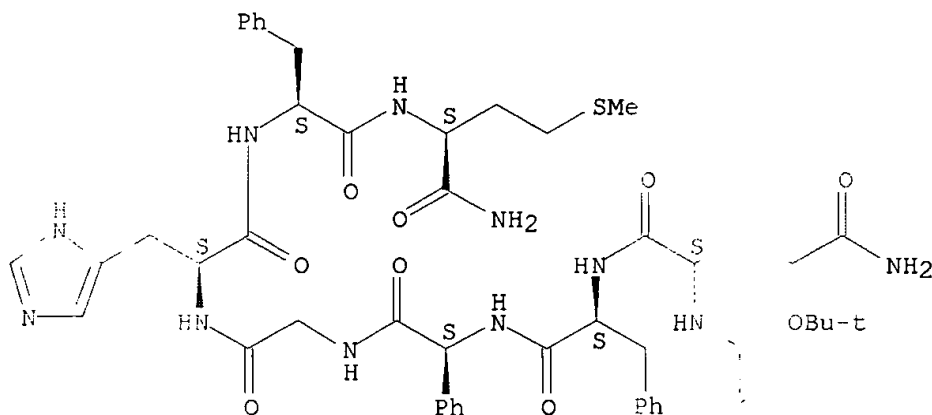


RN 400749-61-3 CAPLUS

CN L-Methioninamide, N2-[(1,1-dimethylethoxy)carbonyl]-L-glutaminy-L-phenylalanyl-(2S)-2-phenylglycylglycyl-L-histidyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).





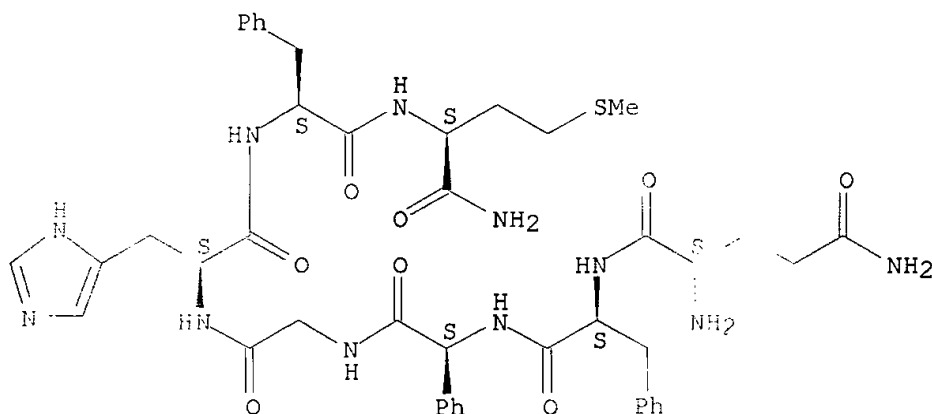
IT 400747-92-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of substance P and litorin analogs by peptide coupling)

RN 400747-92-4 CAPLUS

CN L-Methioninamide, L-glutaminyl-L-phenylalanyl-(2S)-2-phenylglycylglycyl-L-histidyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB With the aim of obtaining new biol. active compds., we have synthesized nine combined peptides (I)-(IX) consisting of combinations of the C-terminal tripeptide litorin and the hydrophobic central fragments of substance P, and also modified analogs of them. The synthesis of these compds. was achieved by the methods of classical peptide chem. with the condensation of their N-terminal moieties with the C-terminal tripeptide H-His-Phe-Met-NH<sub>2</sub>.

L4 ANSWER 16 OF 148 CAPLUS COPYRIGHT 2002 ACS

AN 2001:416788 CAPLUS

DN 135:18553

TI Vaccine for the prevention and treatment of Alzheimer's and amyloid related diseases

IN Chalifour, Robert; Hebert, Lise; Kong, Xiangqi; Gervais, Francine

PA Neurochem Inc., Can.

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

|    | PATENT NO.    | KIND   | DATE     | APPLICATION NO.  | DATE     |
|----|---------------|--|----------|------------------|----------|
| PI | WO 2001039796 | A2   | 20010607 | WO 2000-CA1413   | 20001129 |
|    | WO 2001039796 | A3   | 20011206 |                  |          |
|    | W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                  |          |
|    | RL:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |          |                  |          |
|    |               |  |          | US 1999-168594PP | 19991129 |
|    |               |  |          | US 2000-724842 A | 20001128 |
| BR | 2000016022    | A  | 20020806 | BR 2000-16022    | 20001129 |
|    |               |  |          | US 1999-168594PP | 19991129 |
|    |               |  |          | US 2000-724842 A | 20001128 |
|    |               |  |          | WO 2000-CA1413 W | 20001129 |
| EP | 1235587       | A2   | 20020904 | EP 2000-981111   | 20001129 |
|    | R:            | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |          |                  |          |
|    |               |  |          | US 1999-168594PP | 19991129 |
|    |               |  |          | US 2000-724842 A | 20001128 |
|    |               |  |          | WO 2000-CA1413 W | 20001129 |
| NO | 2002002531    | A  | 20020712 | NO 2002-2531     | 20020528 |
|    |               |  |          | US 1999-168594PP | 19991129 |
|    |               |  |          | US 2000-724842 A | 20001128 |
|    |               |  |          | WO 2000-CA1413 W | 20001129 |

## PATENT FAMILY INFORMATION:

FAN 2002:510135

|    | PATENT NO.    | KIND   | DATE     | APPLICATION NO.   | DATE     |
|----|---------------|--|----------|-------------------|----------|
| PI | US 2000094335 | A1   | 20020718 | US 2001-867847    | 20010529 |
|    |               |  |          | US 1999-168594PP  | 19991129 |
|    |               |  |          | US 2000-724842 A2 | 20001128 |
| WO | 2001096937    | A2   | 20021205 | WO 2002-CA763     | 20020529 |
|    | W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                   |          |
|    | RL:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                   |          |
|    |               |  |          | US 2001-867847 A  | 20010529 |

IT 342878-09-5P

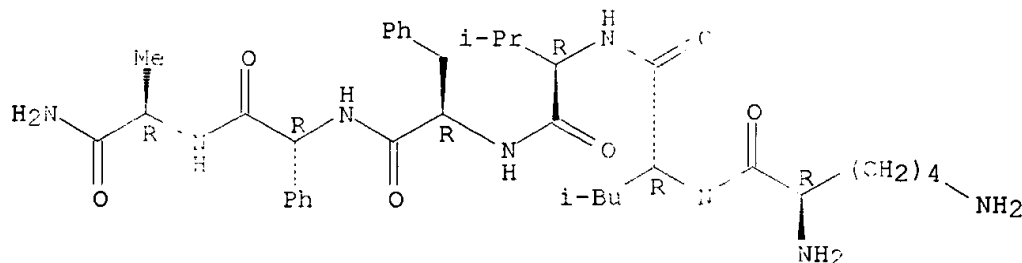
RL: BA (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(vaccine for prevention and treatment of Alzheimer's and amyloid related diseases using all-D peptides that elicit immune response to amyloid protein)

RN 342878-09-5 CAPLUS

CN D-Alaninamide, D-lysyl-D-leucyl-D-valyl-D-phenylalanyl-(2R)-2-phenylglycyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The present invention relates to a stereochem. based "non-self" antigen vaccine for the prevention and/or treatment of Alzheimer's and other amyloid related diseases. The present invention provides a vaccine for the prevention and treatment of Alzheimer's and other amyloid related diseases, which overcomes the drawback assocd. with using naturally occurring peptides, proteins or immunogens.

L4 ANSWER 17 OF 148 CAPLUS COPYRIGHT 20 3 ACS

AN 2001:4 2340 CAPLUS

DN 135:231899

TI Discovery of potent and selective phenylalanine derived CCR3 receptor antagonists. Part 2

AU Dhanak, D.; Christmann, L. T.; Darcy, M. G.; Keenan, R. M.; Knight, S. D.; Lee, J.; Ridgers, L. H.; Sarau, H. M.; Shah, D. H.; White, J. R.; Zhang, L.

CS SmithKline Beecham Pharmaceuticals, Collegeville, PA, 19426-0989, USA

SO Bioorganic & Medicinal Chemistry Letters (2001), 11(11), 1445-1450

CODEN: BMCLE8; ISSN: 0960-894X

PR Elsevier Science Ltd.

DT Journal

LA English

IT 269064-22-4P

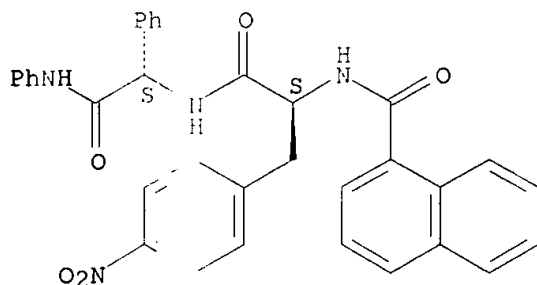
RL: RA (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SYN (Synthetic preparation); THU (Therapeutic use); BCOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(discovery of potent and selective phenylalanine derived CCR3 receptor antagonists)

RN 269064-22-4 CAPLUS

CN Glycinamide, N-(1-naphthalenylcarbonyl)-4-nitro-L-phenylalanyl-N,2-diphenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Highly potent CCR3 antagonists have been developed from a previously reported series of phenylalanine ester-based leads. Soln.-phase, parallel synthesis optimization was utilized to identify highly potent, functional CCR3 antagonists.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 2001:0611 CAPLUS

DN 134:266552

TI First and Second Generation Total Synthesis of the Teicoplanin Aglycon

AU Boger, Dale L.; Kim, Seong Heon; Mori, Yoshiki; Meng, Jian-Hui; Rogel, Olivier; Castle, Steven L.; McAtee, J. Jeffrey

CS Department of Chemistry, The Scripps Research Institute, The Skaggs Institute for Chemical Biology, La Jolla, CA, 92037, USA

SO Journal of the American Chemical Society (2001), 123(9), 1862-1871  
CODEN: JACSAT; ISSN: 0002-7863

PE American Chemical Society

DT Journal

LA English

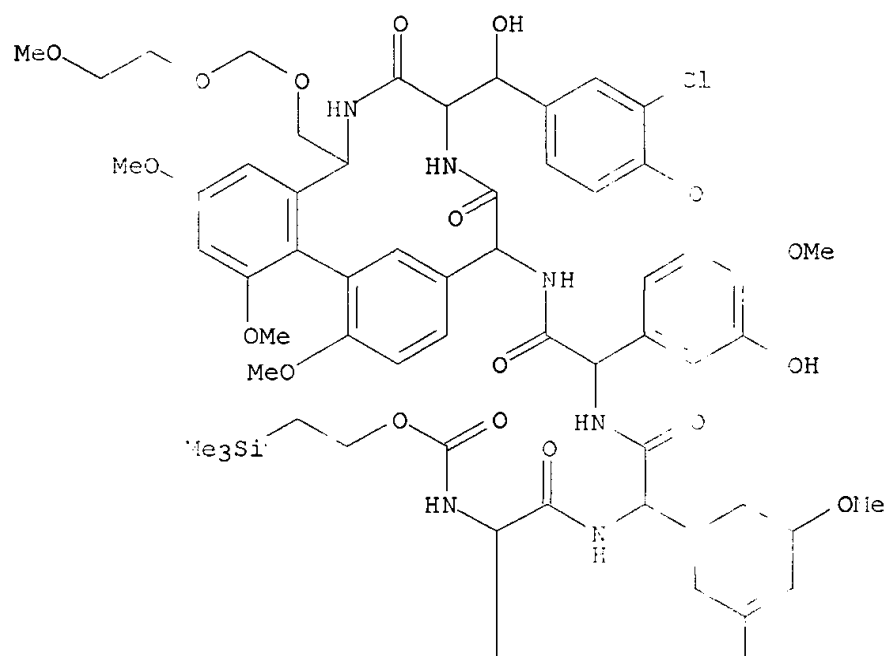
OS CASREACT 134:266552

IT 296781-63-0P 331731-43-2P 331731-45-4P

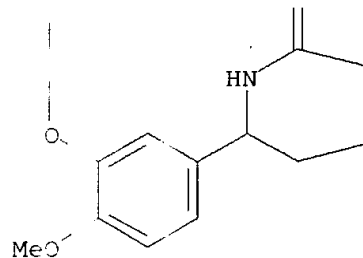
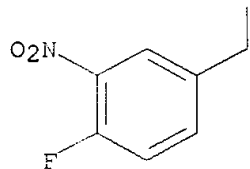
RL: R (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(first and second generation total synthesis of the teicoplanin aglycon)

RN 296781-63-0 CAPLUS

CN L-Tyrosine, 4-fluoro-3-nitro-N-[[2-(trimethylsilyl)ethoxy]carbonyl]-D-phenylalanyl-(2S)-2-[3-[5-[(1R)-1-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-(phenylmethoxy)ethyl]-2-methoxyphenoxy]-5-methoxyphenyl]glycyl-(2R)-2-(3,5-dihydroxy-4-methoxyphenyl)glycyl-(2R)-2-[2'-[(1S)-1-amino-2-[(2-methoxyethoxy)methoxy]ethyl]-4',6',6'-trimethoxy-1,1'-biphenyl]-3-yl]glycyl-3-chloro-β-hydroxy-, (5S)-lactam, cyclic (3S,4S)-ether, stereoisomer (9CI) (CA INDEX NAME)



PAGE 2-A



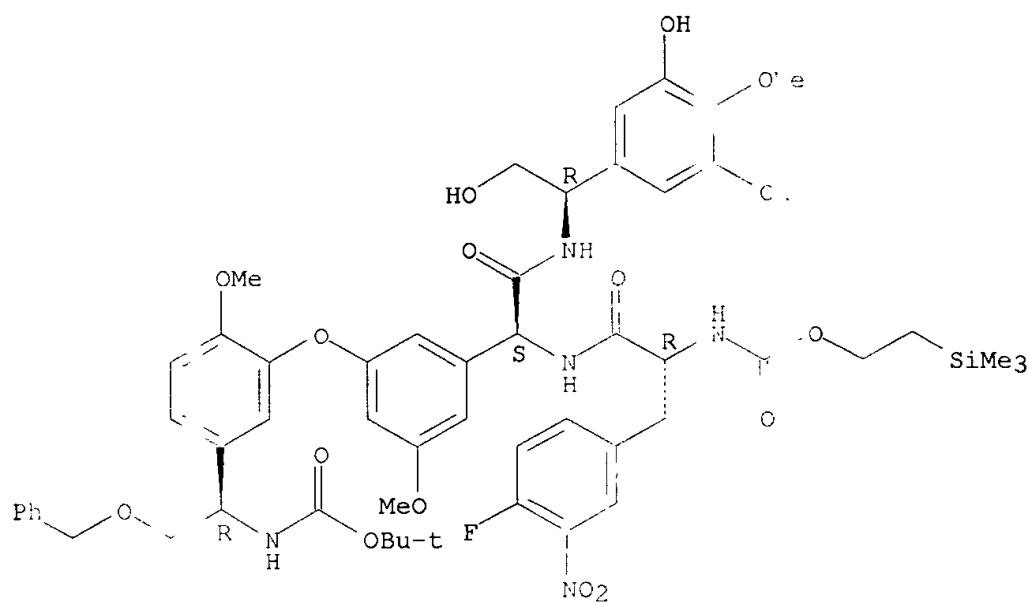
PAGE 2-B

$$-\text{OBu-t}$$
COc1ccccc1

RN 331731 43-2 CAPLUS

CN Glycin mide, 4-fluoro-3-nitro-N-[(2-(trimethylsilyl)ethoxy)carbonyl]-D-phenyl lanyl-N-[(1R)-1-(3,5-dihydroxy-4-methoxyphenyl)-2-hydroxyethyl]-2-[3-[5-(1R)-1-[[ (1,1-dimethylethoxy) carbonyl] amino]-2-(phenylmethoxy)ethyl]-2-methoxyphenoxy]-5-nitroxyphenyl]-, (2S)- (9CI)  
(CA IN EX NAME)

Absolute stereochemistry. Rotation (+).

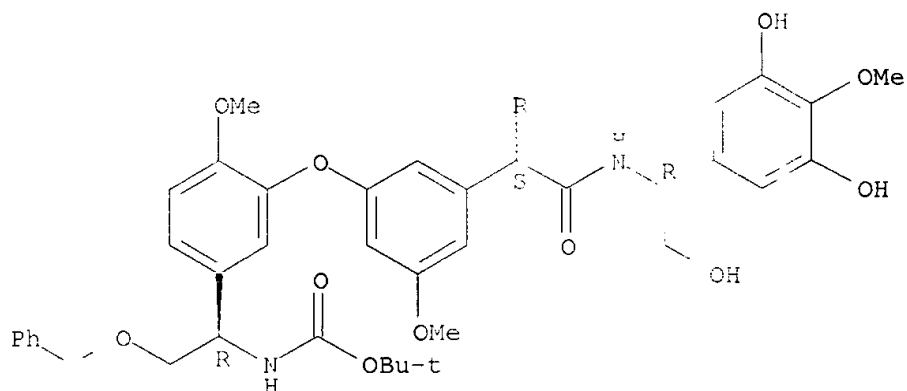


RN 331731 45-4 CAPLUS

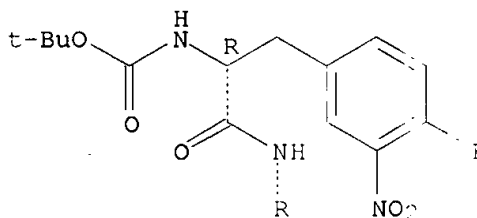
CN Glycin mide, N-[(1,1-dimethylethoxy)carbonyl]-4-fluoro-3-nitro-D-phenyl lanyl-N-[(1R)-1-(3,5-dihydroxy-4-methoxyphenyl)-2-hydroxyethyl]-2-[3-{5-[(1R)-1-[(1,1-dimethylethoxy)carbonyl]amino]-2-(phenylmethoxy)ethyl}-2-methoxyphenoxy]-5-methoxyphenyl]-, (2S)- (9CI)  
(CA II: EX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A

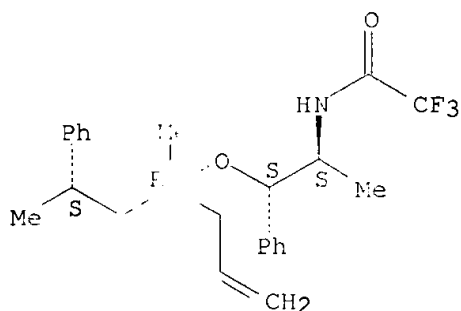


AB Full details of studies leading to the total synthesis of the teicoplanin aglycon are provided. Key elements of the first generation approach (26 steps from constituent amino acids, 1% overall) include the coupling of an EFG tripeptide precursor to the common vancomycin/teicoplanin ABCD ring system and sequential DE macrocyclization of the 16-membered ring with formation of the diaryl ether via a phenoxide nucleophilic arom. substitution of an o-fluoronitroarom. (80%, 3:1 atropisomer diastereoselection) followed by 14-membered FG ring closure by macrolactamization (66%). Subsequent studies have provided a second generation total synthesis which is shorter, more convergent, and highly diastereoselective (22 steps, 2% overall). This was accomplished by altering the order of ring closures such that FG macrolactamization (95%) preceded coupling of the EFG tripeptide to the ABCD ring system and subsequent DE ring closure. Notably, DE macrocyclization via diaryl ether formation on the key intermediate in the latter approach incorporating the intact FG ring system occurred with exceptional diastereoselection for formation of the natural atropisomer (>10:1, 76%) without problematic C23 epimerization provided the basicity of the reaction is minimized.

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE PDF FORMAT

L4 ANSWER 19 OF 148 CAPLUS COPYRIGHT 2003  
AN 2001:57805 CAPLUS  
DN 134:252075  
TI Synthesis of enantiopure homoallylic ethers by reagent controlled facial selective allylation of chiral ketones  
AU Tietze, Lutz F.; Weigand, Berthold; Volker, Ludwig; Wulff, Christian; Bittner, Christian  
CS Institut für Organische Chemie Georg-August Universität Göttingen, Göttingen, 37077, Germany  
SO Chemistry--A European Journal (2001), 7(1), 161-168  
CODEN: CEUJED; ISSN: 0947-6539  
PB Wiley-VCH Verlag GmbH  
DT Journal  
LA English  
OS CASREACT 134:252075  
IT 330798-68-0P 330798-69-1P  
RL: BYP (Byproduct); SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of enantiopure homoallylic ethers by reagent controlled facial selective allylation of chiral ketones)  
RN 330798-68-0 CAPLUS  
CN Acetamide, 2,2,2-trifluoro-N-[(1S,2S)-1-methyl-2-[[[(1R)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl] (9CI) (CA INDEX NAME)

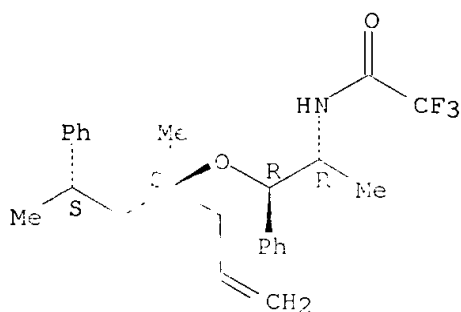
Absolute stereochemistry.



RN 330798-69-1 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[[(1S)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]-2,2,2-trifluoro-N-(acetamido)ethane-1-carboxamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 330798-62-4P 330798-63-5P 330798-73-7P

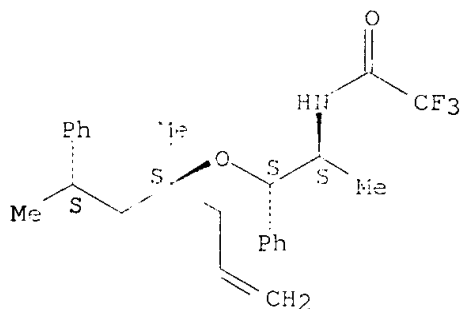
330798-76-0P

RL: SPW (Synthetic preparation); PREP (Preparation)  
(synthesis of enantiopure homoallylic alcohols by reagent controlled  
facial selective allylation of chiral ketones)

RN 330798-62-4 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1S,2S)-1-methyl-2-[[[(1S)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl]-2,2,2-trifluoro-N-(acetamido)ethane-1-carboxamide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

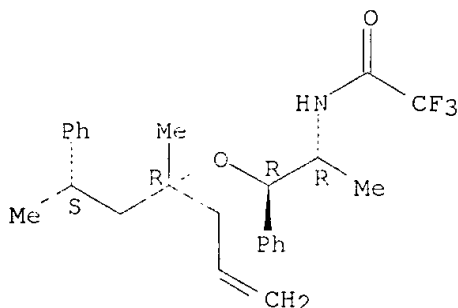


RN 330798-63-5 CAPLUS



CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl (9CI) (CA INDEX NAME)

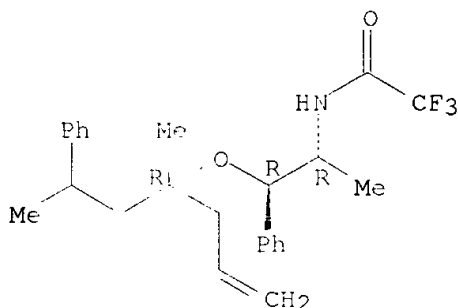
Absolute stereochemistry. Rotation (+).



RN 330798-73-7 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl (9CI) (CA INDEX NAME)

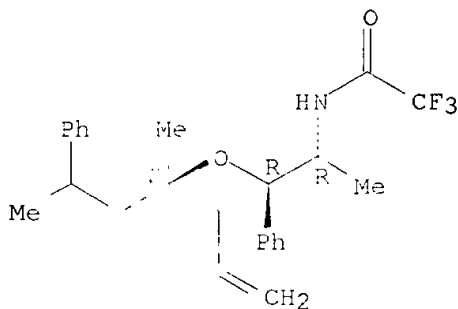
Absolute stereochemistry.



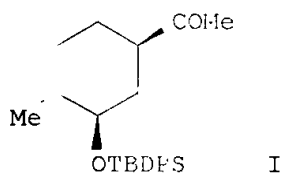
RN 330798-76-0 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-1-[(2S)-2-phenylpropyl]-3-butenyl]oxy]-2-phenylethyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



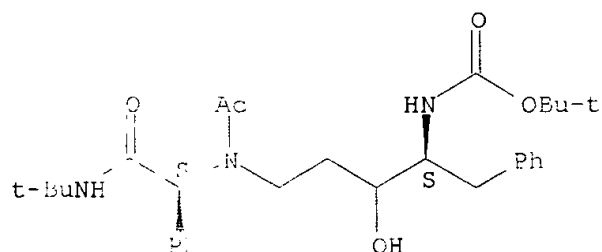
RE.CNT 64      THERE ARE 64 CITED REFERENCES FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THIS DAT

L4 ANSWER 10 OF 148 CAPLUS COPYRIGHT 1988  
AN 2000:732035 CAPLUS  
DN 133:282086  
TI Preparation of non-peptidyl dipeptides as HIV protease inhibitors  
IN Nakamura, Yuji; Takagi, Eiji; Ozawa, Yoji; Miyama, Akiko  
PA Sankyo Co., Ltd., Japan  
SO Jpn. Kokai Tokkyo Koho, 29 pp.  
CODEN: JKKXXAF  
DT Patent  
LA Japanese  
FAN.CNT 1

|    | PATENT NO.    | KIND | DATE     | INVENTION NO. | DATE     |
|----|---------------|------|----------|---------------|----------|
| PI | JP 2000090242 | A2   | 20001017 | 47536         | 19990405 |
|    |               |      |          | 47536         | 19990405 |

|    |   |   |
|----|---|---|
| OS | MARPAT 133:282086   |   |
| IT | 251339-75-0P 300351-43-3P 300351-51-3P<br>300351-53-5P 300351-56-8P 300351-59-1P<br>300351-67-1P  |   |
|    | RL: BAC (Biological activity or effect study, unclassified); SPN (Synthetic peptide); BICI (Biological study); PREP (Preparation of prepn. of non-peptidyl dipeptide) for prevention or treatment of AIDS.        | pt adverse); BSU (Biological study); THU (Therapeutic use); SES (Uses)<br>HIV protease inhibitors |
| RN | 251339-75-0 CAPLUS  |   |
| CN | D-glycero-Pentitol, 5-[acetyl[(1S)-1-(ethylethyl)amino]-2-oxo-1-phenylethyl]amino]-1,2,4,5-tetrahydro-2H-pyridine-2-thioxo-1,4-dione-1-methyl-2-methoxy carbonyl]amino]-1-phenyl-1H-imidazole-5-carboxamide (9CI) | (CA INDEX NAME)   |

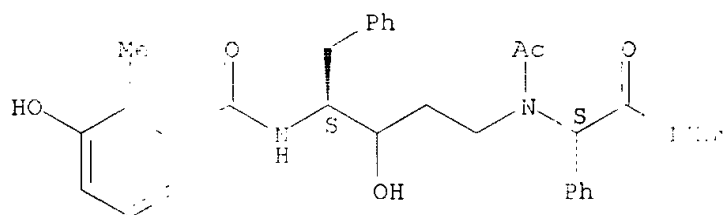
Absolute stereochemistry.



RN 300351-13-3 CAPLUS

CN D-glycero-Pentitol, 5-[acetyl[(1S)-2-oxo-1-phenyl-2-[(phenylmethyl)amino]ethyl]amino]-1,2,4,5-tetrahydroxy-2-methylbenzoyl)amino]-1-phenyl-, (3.xi.)- (9CI) (CA INDEX NAME)

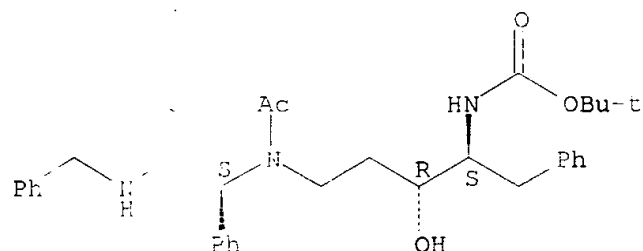
Absolute stereochemistry.



RN 300351-51-3 CAPLUS

CN D-erythro-Pentitol, 5-[acetyl[(1S)-2-oxo-1-phenyl-2-[(phenylmethyl)amino]ethyl]amino]-1,2,4,5-tetrahydroxy-2-[(1,1-dimethylethoxy)carbonyl]amino]-1-phenyl-, (3.xi.)- (CA INDEX NAME)

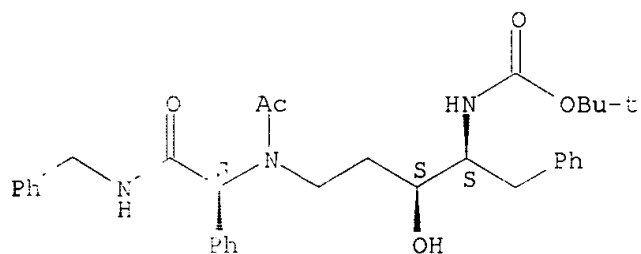
Absolute stereochemistry.



RN 300351-13-5 CAPLUS

CN L-threo-Pentitol, 5-[acetyl[(1S)-2-oxo-1-phenyl-2-[(phenylmethyl)amino]ethyl]amino]-1,2,4,5-tetrahydroxy-2-[(1,1-dimethylethoxy)carbonyl]amino]-1-phenyl-, (3.xi.)- (CA INDEX NAME)

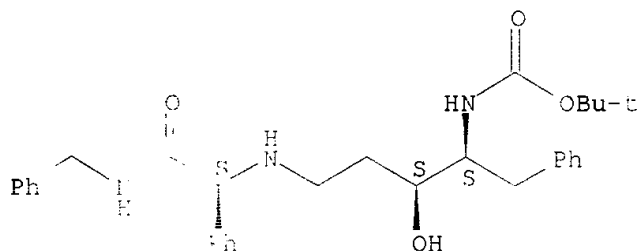
Absolute stereochemistry.



RN 300351-56-8 CAPLUS

CN L-threo-Pentitol, 1,2,4,5-tetradeoxy-2-[(1-phenyl-2-  
 [(phenylmethyl)amino]ethyl)amino]-1-phenyl-2-  
 (9CI) (CA INDEX NAME)

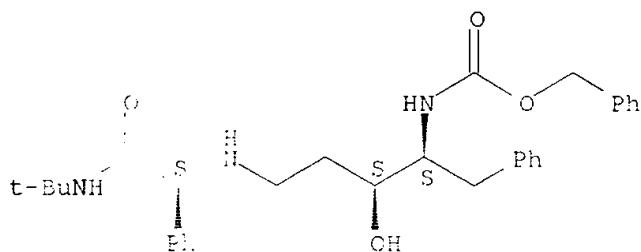
Absolute stereochemistry.



RN 300351-59-1 CAPLUS

CN L-threo-Pentitol, 1,2,4,5-tetradeoxy-2-[(1,1-dimethylethyl)amino]-  
 2-[(1-phenylethyl)amino]-1-phenyl-2-[(1-phenylmethoxy)carbonyl]amino]-  
 (9CI) (CA INDEX NAME)

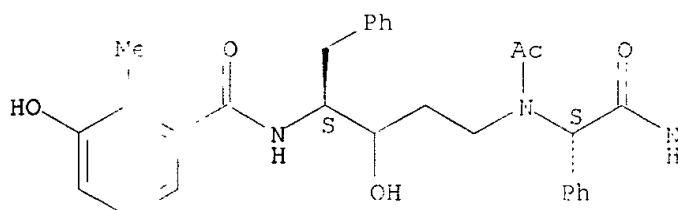
Absolute stereochemistry.



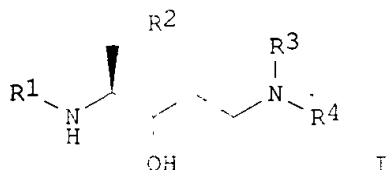
RN 300351-67-1 CAPLUS

CN D-glycero-Pentitol, 5-[acetyl[(1S)-2-[(1-phenyl-2-  
 [(phenylmethyl)amino]ethyl)amino]-1,2,4,5-tetradeoxy-2-[(3-hydroxy-2-  
 methylbenzoyl)amino]-1-phenyl-2-[(1-phenylmethoxy)carbonyl]amino]-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB The title compds. (I; R1 = (un)substituted alkyl, aralkyloxycarbonyl, or arylcarbonyl; R2 = H, (un)substituted C1-10 alkyl, C2-15 aralkylsulfonyl; R4 = (un)substituted C1-10 alkyl, C2-15 aralkyl, C6-14 aryl, or C7-15 aralkyl; R6 = HCOCHR5; wherein R5 = (un)substituted C1-10 alkyl, C6-14 aryl, or C7-15 aralkyl; R6 = (un)substituted C1-6 alkyl, C3-8 cycloalkyl], pharmacol. acceptable salts thereof, or prodrugs thereof, which are useful for the prevention or treatment of HIV infection. Thus, (1S,2S)-4-[acetyl-((1S)-1-(tert-butyl)-2-naphthyl)ethyl]amino]-1-benzyl-2-hydroxy-3-(3-hydroxy-2-methylbenzoic acid using dimethylaminopropyl)carbodiimide hydrate and Et3N at room temp. for 12 h, followed by aq. NaOH and MeOH to give N-[(1S,2S)-4-(tert-butylcarbamoyl)-2-((R)-1-naphthyl)ethyl]-1-benzyl-2-hydroxy-2-methylbenzamide (II). II is active against recombinant HIV protease.

L4 ANSWER 21 OF 148 CAPLUS COPYRIGHT 2

AN 2000:641342 CAPLUS

DN 13:238713

TI Preparation of ketones and amides as

IN Dhonak, Lashyant; Knight, Steven D.

PA SmithKline Beecham Corporation, USA

SO PC Int. Appl., 26 pp.

COLEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| PATENT NO.  | KIND | DATE     |
|-------------|------|----------|
| WO 00003172 | A1   | 20000914 |

W: A, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, UA, YU

receptor antagonists

| APPLICATION NO. | DATE     |
|-----------------|----------|
| -US5911         | 20000308 |

B, GR, IE, IT, LU, MC, NL,

PT, SE

-123232PP 19990308

-123245PP 19990308

OS MAPAT 133:238323

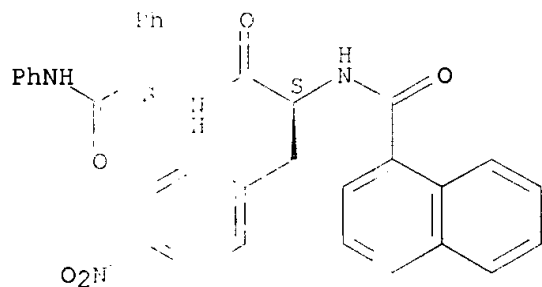
IT 269064-22-4P

RL: BAC (Biological activity or effect); SPN (Synthetic preparation); THU (Therapeutic use); PREP (Preparation); USES (Uses)

RN 269064-22-4 CAPLUS

CN Glutathione, N-(1-naphthalenylcarbonyl)-L-phenyl-, (2S)- (HCl) (CA INDEX NAME)

Absolute stereochemistry.



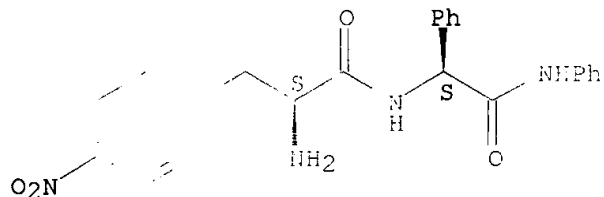
IT 269064-53-1

RL: RCT (Reactant); RACT (Reactant or product); THU (Therapeutic use); PREP (Preparation); USES (Uses)

RN 269064-53-1 CAPLUS

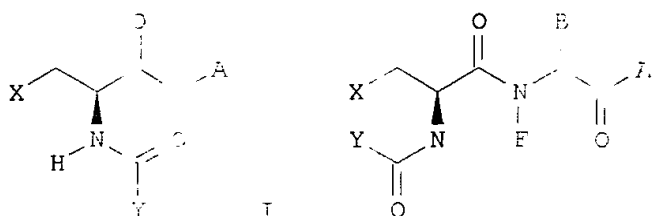
CN Glutathione, 4-nitro-L-phenylalanyl-N,2-diphenyl-, monohydrochloride, (2S)- (HCl) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

GI

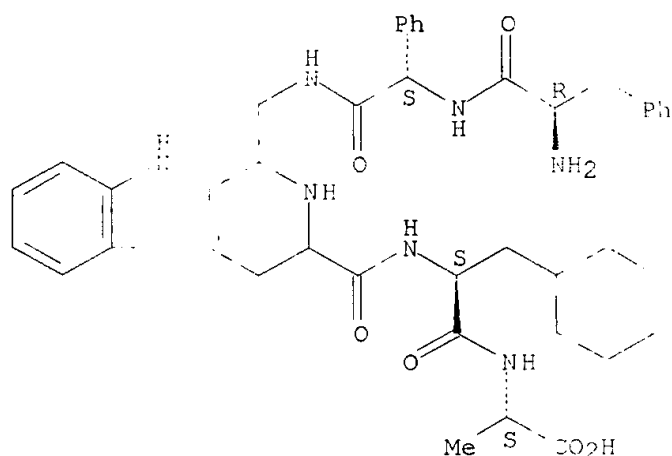


AB The title compds. [I or II; A = OR<sup>1</sup>, alkylaryl, etc.; X = (un)substituted aryl, heteroaryl; B = H, Me, aryl, etc.] are receptor antagonists useful in treating allergic disease, were prepd. and formulated. E.g. a 3-step synthesis of [A = OPh; X = 4-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>; Y = 1-phenyl] was given. Compds. I or II are effective at 0.01-40 mg/kg/day (oral administration).

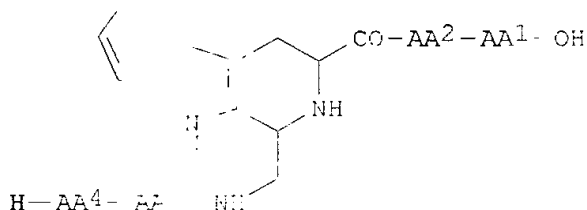
RE.CNT 4 THERE ARE 4 CITED REFERENCES. ALL CITATIONS AVAILABLE IN THE FORMAT

L4 ANSWER 22 OF 148 CAPLUS COPYRIGHT 2000: 9236 CAPLUS  
 AN 2000: 9236 CAPLUS  
 DN 133:310131  
 TI Solid-phase synthesis of 1,2,3,4-tetrahydro-1- $\beta$ -carboline-containing peptidomimetics  
 AU Li, Xianfeng; Zhang, Lianshan; Zhang, Jie; Hall, Steven E.; Tam, James P.  
 CS Splint Pharmaceuticals A Division of Wyand Company, Cambridge, MA, 02139, USA  
 SO Organic Letters (2000), 2(20), 3075-3076  
 COLEN: ORLEF7; ISSN: 1523-7060  
 PB American Chemical Society  
 DT Journal  
 LA English  
 OS CASREACT 133:310131  
 IT 301850-31-7P  
 RL: S.M. (Synthetic preparation); PREP (Solid-phase synthesis of tetrahydro-1- $\beta$ -carboline-contg. peptidomimetics)  
 RN 301850-31-7 CAPLUS  
 CN L-Alanine, 1,3,4,9-tetrahydro-1-[[[1-phenylglycyl]amino[methyl]-1H-pyridin-2-yl]-2-yl]-2-phenyl-1H-indole-3-carbonyl-3-cyclohexyl-L-alanine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB A solid-phase method for the synthesis of 2,3,4-tetrahydro-beta-carbolines-contg. peptidomimetics I (AA1, AA2 = Ala, Leu, Phe, Pro, Val, Asp, Gly, etc.) has been developed. The key step in the strategy is the Pictet-Spengler condensation of a tryptophan-contg. fragment with an Fmoc-amino aldehyde.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THIS RECORD FORMAT

L4 ANSWER 23 OF 148 CAPLUS COPYRIGHT 2000

AN 2000:08804 CAPLUS

DN 13 10 056

TI Synthetic studies on the DEF ring system of ristocetin A via ruthenium-promoted SNAr reaction: problems and solutions using arylamine-Ru complexes

AU Pearson, Anthony J.; Heo, Jung-Nyoung  
CS Department of Chemistry, Case Western Reserve University, Cleveland, OH, 44106, USA

SO Tetrahedron Letters (2000), 41(32), 5001-5006  
CODEN: TETLEY; ISSN: 0040-4039

PB Elsevier Science Ltd.

DT Journal Article

LA English

OS CAPLUS DT 133:282056



IT 299179-32-1P

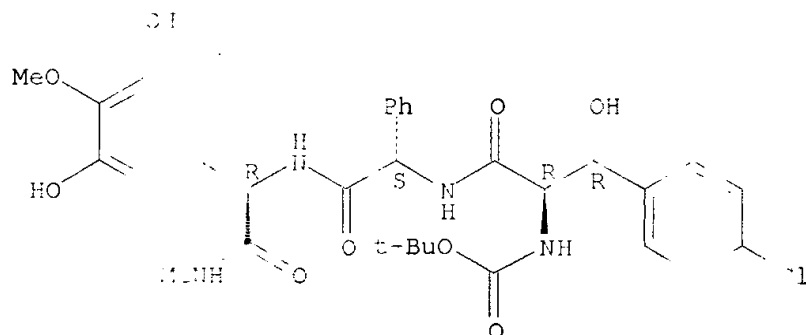
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

Synthetic studies on the DEF ring system of ristocetin A via ruthenium-promoted SNAr reaction using arylserine-Ru complexes)

RN 299179-32-1 CAPLUS

CN Glycylamide, (.beta.R)-4-chloro-N-[(1,1-dimethylethoxy)carbonyl]-.beta.-hydroxy-D-phenylalanyl-(2S)-2-phenylglycyl-2-(3,5-dihydroxy-4-methoxyphenyl)-N-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Ruthenium-promoted intramol. SNAr reaction has allowed the construction of the 10-membered DEF model macrocycle of ristocetin A that incorporates the required arylserine residue as the E ring. The required arylserine was synthesized using the Sharpless asym. hydroxylation reaction starting with (E)-4-chlorocinnamic acid.

RE.CNT 24 HERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THIS RECORD FORMAT

L4 ANSWER 24 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 2000:475632 CAPLUS

DN 133: 64880

T1 Arylalkanoylaminoacetamides as blood clotting factor Xa inhibitors

IN Defossa, Elisabeth; Heinelt, Uwe; Klindler, Otmar; Zoller, Gerhard; Marten, Hans; Al-Obeidi, Fahad D.; Walker, Armin; Wildgoose, Peter

PA Aventis Pharma Deutschland G.m.b.H., Germany

SO PCT Int. appl., 1-0 pp.

CODE: P1XXL2

DT Patent

LA English

FAN.CNT

| PATENT NO.  | KIND | DATE     | PUBLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| PI WO 2000/47548  | A1   | 20000713 | EP 9-EP10341    | 19991223 |
| AC, AL, AM, AT, AU, BA, BE, BG, BR, BY, CA, CH, CN, CR, CU, DE, DK, DM, EE, ES, FI, GE, GH, GM, HR, HU, ID, IL, JP, KE, KG, KP, KR, LC, LK, LR, LS, LT, LU, LV, MA, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TM, TR, TT, TZ, UG, UZ, VN, YU, ZA, ZW, AM, AZ, FY, KG, KZ, MD, RU, TJ, TM, GH, GM, KE, LS, MW, SD, SL, SN, TZ, UG, ZW, AT, BE, CH, CY, DE, EK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, |      |          |                 |          |

CG, CI, CM, GA, GN, GU, ML, NE, SN, TD, TG  
 1 9-100001 A 19990102  
 2 9-119538 A 19991001  
 EP 1002268 A1 20000726 9-100001 19990102  
 1: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO  
 CA 2008581 AA 20000713 A 9-2358581 19991223  
 2 9-100001 A 19990102  
 3 9-119538 A 19991001  
 4 9-EP10341W 19991223  
 BR 9916733 A 20010925 9-16733 19991223  
 2 9-100001 A 19990102  
 3 9-119538 A 19991001  
 4 9-EP10341W 19991223  
 EP 100946 A1 20011117 9-967001 19991223  
 1: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, FI  
 2 9-100001 A 19990102  
 3 9-119538 A 19991001  
 4 9-EP10341W 19991223  
 JP 2002534408 T2 20021015 9-592257 19991223  
 2 9-100001 A 19990102  
 3 9-119538 A 19991001  
 4 9-EP10341W 19991223  
 ZA 2001004772 A 20020513 A 9-4772 20010612  
 2 9-100001 A 19990102  
 NO 2001003141 A 20010803 9-3141 20010622  
 2 9-100001 A 19990102  
 3 9-119538 A 19991001  
 4 9-EP10341W 19991223

OS MARPAT 133:104880

IT 283160-50-9P

RL: FNC (Biological activity or effect, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of arylalkanoylaminoacetamides as blood coagulation factor Xa inhibitors)

RN 283160-50-9 CAPLUS

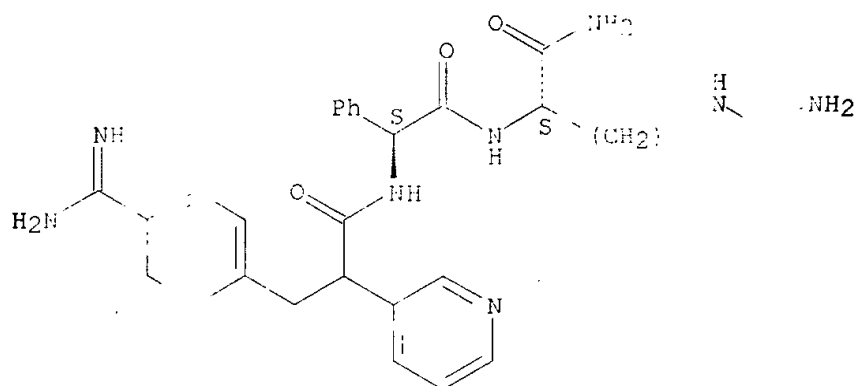
CN L-Ariginamide, (2S)-N-[3-[4-(aminomethyl)phenyl]-1-oxo-2-(3-pyridinyl)propyl]-2-phenylglycyl-, triacetate (9CI) (CA INDEX NAME)

CM

CRN 283160-49-6

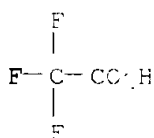
CMF 283160-49-6 H25 N9 O3

Absolute stereochemistry.



CM

CRM 05-1  
CMP H F3 O2



IT 283162-49-6P 283162-22-1P 283162-23-2P

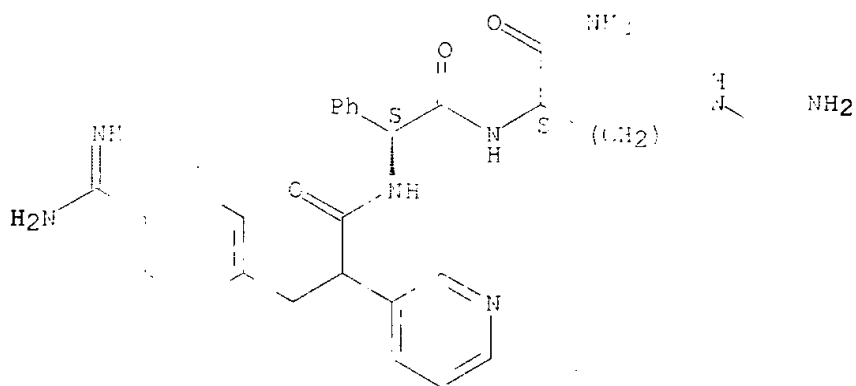
283162-24-3P 283162-25-4P

RL: L-N (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(Group of arylalkanoylaminoacetamides blood coagulation factor Xa inhibitors)

RN 283162-49-6 CAPLUS

CN L-Arylaminamide, (2S)-N-[3-[4-(aminomethyl)phenyl]phenyl]-1-oxo-2-(3-pyridinyl)propyl]-2-phenylglycyl- (9- INDEX NAME)

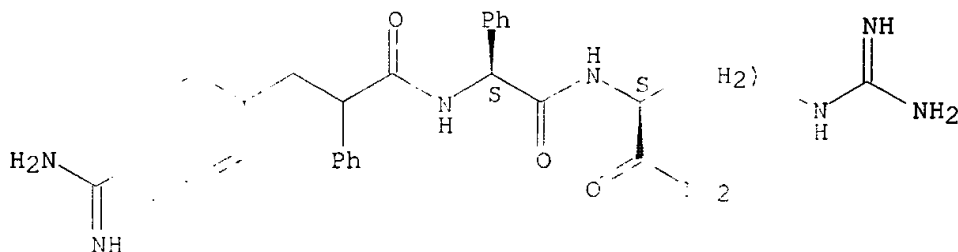
Absolute stereochemistry.



RN 283162-22-1 CAPLUS

CN L-Argininamide, (2S)-N-[3-[4-(aminomethyl)phenyl]-1-oxo-2-phenylpropyl]-2-phenylglycyl- (9CI) (CA EX NAME)

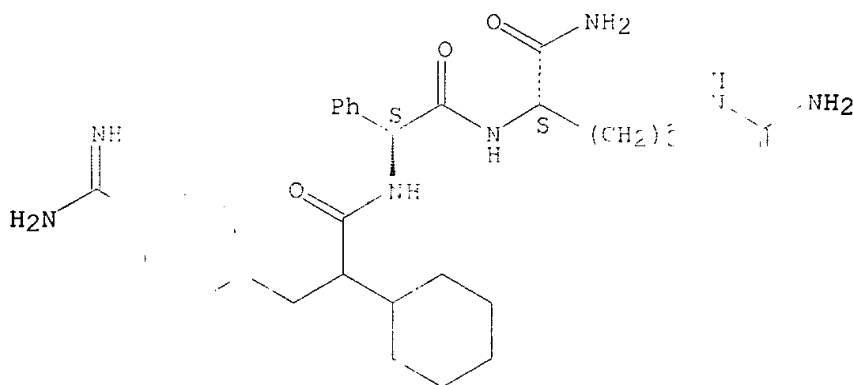
Absolute Stereochemistry.



RN 283162-23-2 CAPLUS

CN L-Argininamide, (2S)-N-[3-[4-(aminomethyl)phenyl]-2-cyclohexyl-1-oxopropyl]-2-phenylglycyl- (9CI) (CA EX NAME)

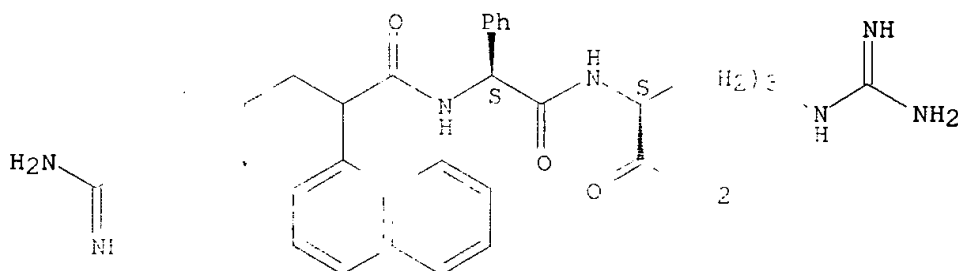
Absolute Stereochemistry.



RN 283162-21-3 CAPLUS

CN L-Argininamide, (2S)-N-[3-[4-(aminomethyl)phenyl]-2-(1-naphthalenyl)-1-oxopropyl]-2-phenylglycyl- (9CI) (CA EX NAME)

Absolute Stereochemistry.

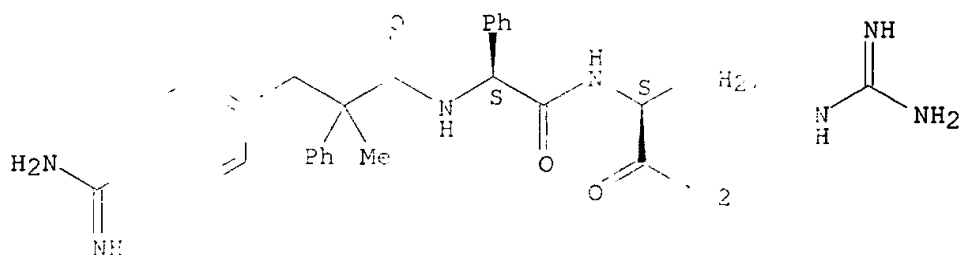


RN 283162-25-4 CAPLUS

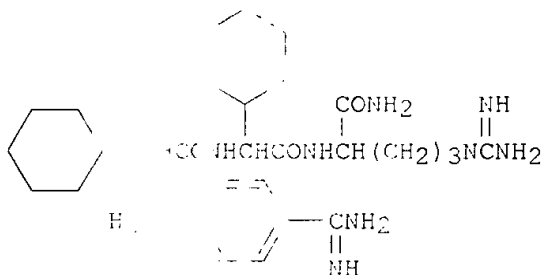
CN L-Argininamide, (2S)-N-[3-[4-(aminomethyl)phenyl]-2-methyl-1-oxo-2-

phenylpropyl]-2-phenylglycyl- (9CI) A (X NAME)

Absolute stereochemistry.



GI



AB Title compds. were prepd. for use as inhibitors of the blood clotting enzyme factor Xa. Thus, the diamide was repd. in a 9-step synthesis. I<sub>50</sub> Ki for factor Xa inhibition of 0.1 μM.

RE.CNT THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RECORD FORMAT

L4 ANNOTATED 5 OF 148 CAPLUS COPYRIGHT 2003 A

AN 2003:47:173 CAPLUS

DN 13:47:18

TI Total synthesis of the teicoplanin aglycone

AU Boeck, Dale L.; Kim, Seong Heon; Miyake, Masumu; Strittmatter, Harald; Wong, Alan-Hui; Mori, Yoshiki; Rogel, Alexander; Castle, Steven L.; McAtee, J. Jeffrey

CS Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA 92037, USA

SO Journal of the American Chemical Society 122(30), 7416-7417

COB: ACSAT; ISSN: 0002-7863

PB American Chemical Society

DT Journal

LA English

IT 296781-63-0P

RI: RCT (Reagent); SPN (Synthetic preparation); PREP (Preparation); RACT (Reagent or reagent)

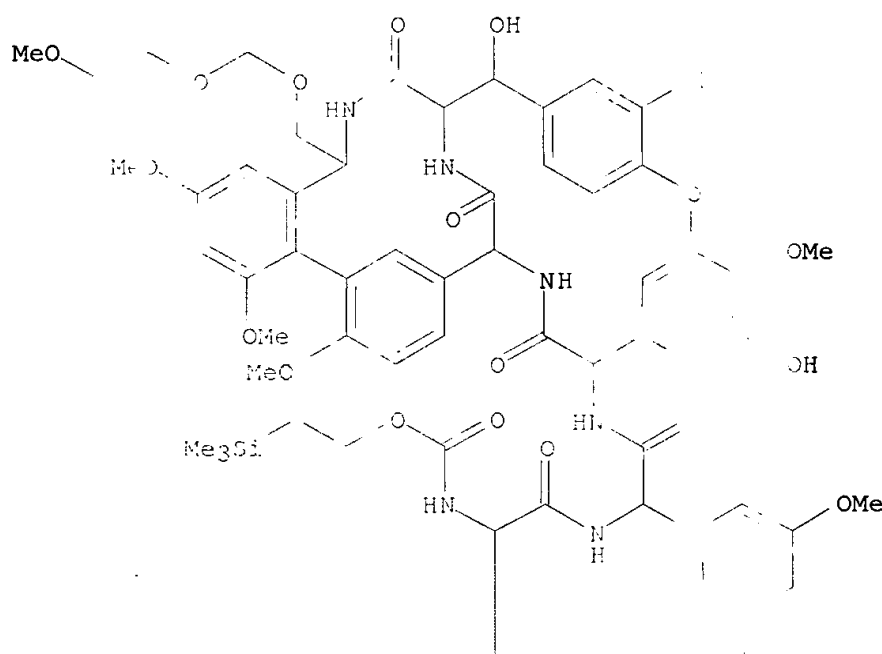
RI: Total synthesis of teicoplanin aglycone

RN 296781-63-0 CAPLUS

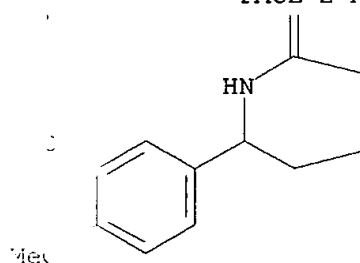
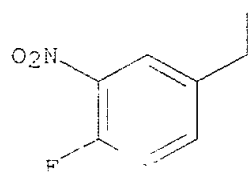
CN L-Serine, 4-fluoro-3-nitro-N-[[2-(trimethylsilyl)ethoxy]carbonyl]-D-

phenylalanyl-(2S)-2-[3-[5-[(1R)-1-[(1S)-1-ethylethoxy)carbonyl]amino]-2-(phenylmethoxy)ethyl]-2-methoxyphenoxy]-2-methoxyphenyl]glycyl-(2R)-2-[3,5-dihydroxy-4-methoxyphenyl]glycyl-(2R)-2-[2-[(1S)-1-amino-2-[(2-methoxyethoxy)methoxy]ethyl]-4',5,6'-trimethoxy[1,1'-biphenyl]-3-yl]glycyl-3-chloro-β-hydroxy-, (5.fwdarw.4) lactam, cyclic (3.fwdarw.54)-ether, stereoisomer (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



PAGE 2-B

OBu-t

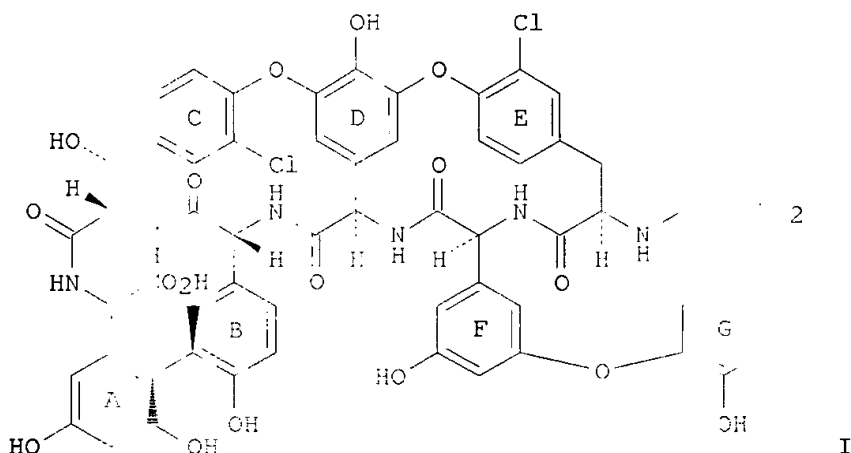
O En

PAGE 2-B

-OBu-t

-O-CH<sub>2</sub>-CH<sub>2</sub>-

GI



AB Teicoplanin is a complex of five antibiotics isolated from *Actinoplanes teichomyceticus* that are related to vancomycin. The first total synthesis of the teicoplanin aglycon (I) is described. Key elements of the approach include sequential DE and FG ring system introductions onto the common vancomycin/teicoplanin ABCD ring system providing a late stage divergent total synthesis of the two classes of glycopeptide antibiotics. The ring systems were introduced enlisting a nucleophilic arom. substitution reaction of an o-fluoronitroarom. for cyclization and formation of the 16-membered DE diaryl ether and a subsequent lactamization of the N-terminus amine for closure of the 14-membered F ring system. The teicoplanin aglycon was obtained in 48% yield identical in all respects with authentic material.

RE.CNT 16 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THIS RECORD

L4 ABSTRACT 26 OF 118 CAPLUS COPYRIGHT 2003

AN 2003:456736 CAPLUS

DN 13:39228

TI Novel malonic acid derivatives, processes for their preparation, their use and pharmaceutical compositions containing them (inhibition of factor Xa activity)

IN De Gossa, Elisabeth; Heinelt, Uwe; Klein, Otmar; Zoller, Gerhard; Matter, Hans; Al-Obeidi, Fahad A.; Walder, Armin; Wildgoose, Peter

PA Aventis Pharma Deutschland G.m.b.H., Germany

SO Eur. Pat. Appl., 76 pp.

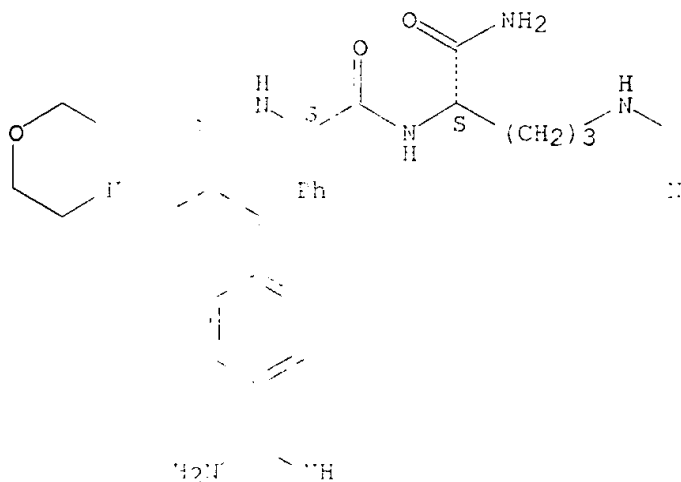
CCPNT: FPXXDW

DT Pat  
LA Eng 131  
FAN.CNT

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| PI EP 011563  | A1   | 20000705 | 9-100002            | 19990102 |
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| CA 2350578  | AA   | 20000713 | 9-2358578           | 19991223 |
| 9-100002 A 19990102   |  |          |                     |          |
| 9-119537 A 19991001   |  |          |                     |          |
| 9-EP10340W 19991223   |  |          |                     |          |
| WC 001040571  | A1   | 20000713 | 9-EP10340           | 19991223 |
| R: AE, AL, AM, AT, AU, AZ, BA, BE, BR, BY, CA, CH, CN, CR, CU, CE, DE, DK, DM, EE, ES, FI, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, LK, LR, LS, LT, LU, LV, MA, MF, MG, MK, MN, MW, MX, NO, PT, RO, RU, SD, SE, SG, SI, SF, SL, TJ, TM, TR, TT, TZ, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BT, KG, KZ, MD, RU, TJ, TM |  |          |                     |          |
| R: GH, GM, KE, LS, MW, SD, SL, S, UG, ZW, AT, BE, CH, CY, DE, DF, EG, FI, FR, GB, GR, IE, IL, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MI, SN, TD, TG  |  |          |                     |          |
| 9-100002 A 19990102   |  |          |                     |          |
| 9-119537 A 19991001   |  |          |                     |          |
| 9-16732 19991223  |  |          |                     |          |
| 9-100002 A 19990102   |  |          |                     |          |
| 9-119537 A 19991001   |  |          |                     |          |
| 9-EP10340W 19991223   |  |          |                     |          |
| 9-964667 19991223   |  |          |                     |          |
| EP 1140878  | A1   | 20011010 | 9-100002 A 19990102 |          |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |  |          |                     |          |
| 9-119537 A 19991001   |  |          |                     |          |
| 9-EP10340W 19991223   |  |          |                     |          |
| JP 20031420   | T2   | 20021015 | 10-592279           | 19991223 |
| 9-100002 A 19990102   |  |          |                     |          |
| 9-119537 A 19991001   |  |          |                     |          |
| 9-EP10340W 19991223   |  |          |                     |          |
| US 646673   | B1   | 20020528 | 9-473053            | 19991228 |
| 9-100002 A 19990102   |  |          |                     |          |
| 9-119537 A 19991001   |  |          |                     |          |
| NC 0002983  | A  | 20010615 | 1-2983              | 20010615 |
| 9-100002 A 19990102   |  |          |                     |          |
| 9-119537 A 19991001   |  |          |                     |          |
| 9-EP10340W 19991223   |  |          |                     |          |
| OS  | M/F 131189.28  |          |                     |          |
| IT  | 280553-99-3P 280554-02-1P 280554-07-6P   |          |                     |          |
| R: M (Biological activity or effect); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BLS (Biological study); PREP (Preparation); USES (Uses)   |  |          |                     |          |
| RN  | 280553-99-3 APLUS  |          |                     |          |
| CN  | L-phenylalanine, (2S)-N-[2-[[4-(aminomethyl)phenyl]methyl]-3-(4-methylphenyl)-1,3-dioxopropyl]-2-phenyl- (9CI) (CA INDEX NAME) |          |                     |          |

Absolute stereochemistry.

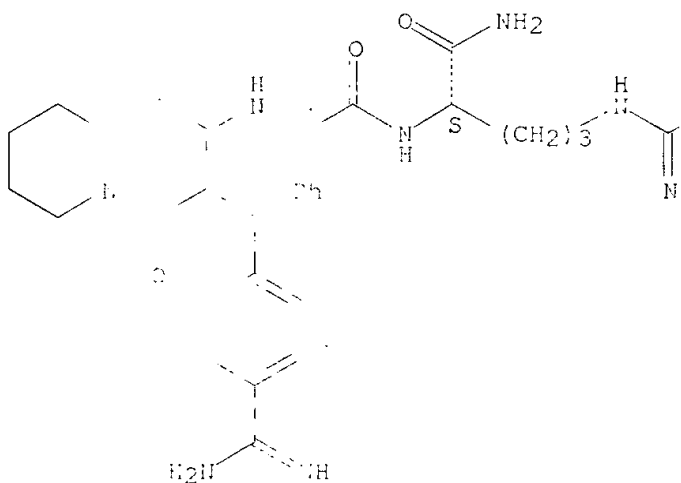




RN 28 11-02-1 LAPLUS

CN L-phenylalaninamide, (2S)-N-[[2-[[[4-(aminomethyl)phenyl]methyl]-1,3-dioxo-3-phenylpropyl]-2-phenylglycyl]-(4-aminomethyl)phenyl]-1,3-dioxo-3-phenylpropyl-L-phenylalaninamide (CA INDEX NAME)

Absolute stereochemistry.



RN 28 11-07-6 LAPLUS

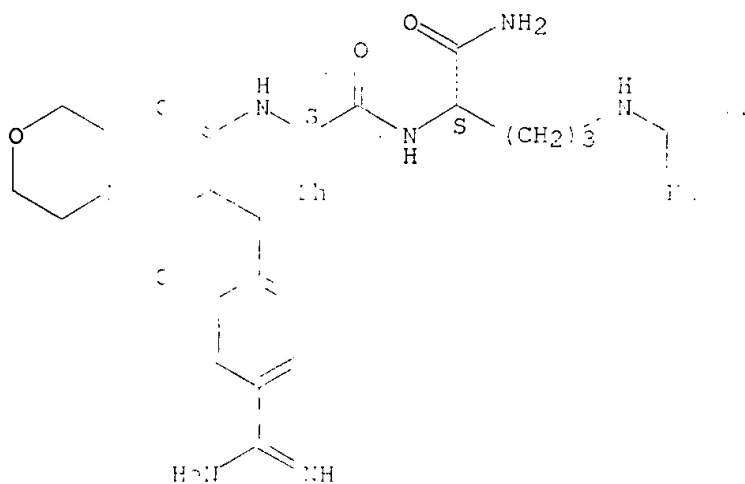
CN L-phenylalaninamide, (2S)-N-[[2-[[[4-(aminomethyl)phenyl]methyl]-1,3-dioxo-3-phenylpropyl]-2-phenylglycyl]-(4-aminomethyl)phenyl]-1,3-dioxo-3-phenylpropyl-L-phenylalaninamide, mono(trifluoroacetate) (CA INDEX NAME)

CF

CF 30553-94-3

CF C29 H39 N3 O5

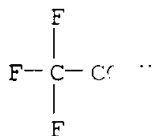
Absolute stereochemistry.



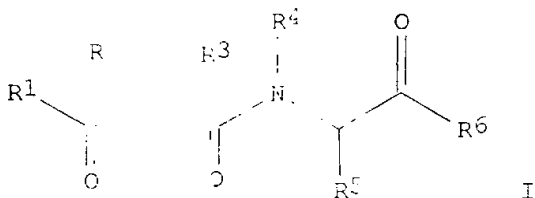
CH

CH 76-05-1

CH Cl H F3 G2



GI



I

AB The present invention relates to the preparation of new compds. for the inhibition of blood clotting proteins, more particularly, to malonic acid derivs., I (R1 = organoamino, organoalkoxy, etc.; R2 = H, C1-4 alkyl; R3 = (un)substituted C6-10-aryl-C1-4-alkyl, C1-4-cycloalkyl, C3-7-cycloalkyl-C1-4-alkyl, C1-10-alkyl, C3-7-cycloalkyl, C3-7-cycloalkyl-C1-4-alkyl, etc.; R4R5 = organoalkoxy, organoalkyl, etc.). Thus, 2-(R,S)-(4-aminobenzyl(piperidin-4-ylcarbonyl)malonamide salt was prepd. in several steps from [1,3]dioxane-4,6-dione and 4-aminobenzonitrile. I are inhibitors

(orally given) of the blood clotting factor Xa. The invention relates to processes for the preparation of a activity and of inhibiting the activity of factor Xa for the treatment and prophylaxis of diseases which can be treated or prevented by the inhibition of factor Xa, and to the use of the compound of formula I in admixt. or otherwise in a pharmaceutical compns. containing pharmaceutically acceptable carrier substances.

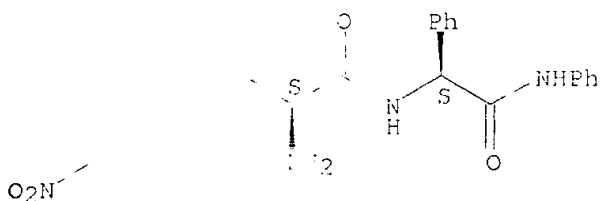
The invention further relates to compns. of formula I together with an inert carrier, in admixt. or otherwise in a pharmaceutical compns. containing pharmaceutically acceptable carrier substances and auxiliary

RE.CNT. THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN FULL FORMAT

L4 AC 1997 07 18 CAPLUS COPYRIGHT  
AN 20 19 871 CAPLUS  
DN 13 04 94  
TI Preparation of phenylalanine amide derivatives as CCR-3 receptor  
a. lists  
IN L. A. Dashyent  
PA S. K. Beecham Corporation, USA  
SO P. Appl., 27 pp.  
C. INDEXED2  
DT P. A.  
LA E. A.  
FAN.CIT

| PI  | NO.   | KIND | DATE     | ATION NO. | DATE     |
|---|---|------|----------|-----------|----------|
| PI  | 27800   | A1   | 20000518 | 2-US26382 | 19991109 |
| CA, JP, US  |   |      |          |           |          |
| AT, BE, CH, CY, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, IT, SE                          |   |      |          |           |          |
| R-107717PP 19981109   |   |      |          |           |          |
| OS  | M. W. 32:347945   |      |          |           |          |
| IT  | 262664-53-1P  |      |          |           |          |
| ACT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) |   |      |          |           |          |
| prepn. of the phenylalanine amide derivatives (CCR-3 receptor antagonists)                  |   |      |          |           |          |
| RN  | CAPLUS  |      |          |           |          |
| CN  | amide, 1-nitro-L-phenylalanyl-L-phenyl-, monohydrochloride, (CA INDEX NAME) |      |          |           |          |

Absolute Stereochemistry.

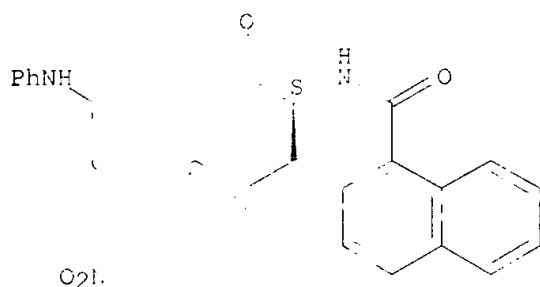


HCl

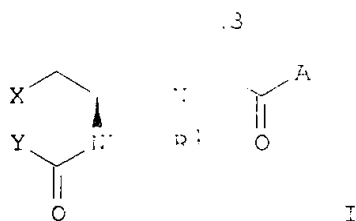
R: (P) Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 (Preparation); USES (Uses, e.g., treatment of phenylalanine amide derivatives); CCR-3 receptor antagonists)

CN G. amide, N-(1-naphthalenylcarbonyl)-D-pro-L-phenylalanyl-N,2-

Absol' Biochemistry.



GI



AB 1. Aminoamide derivs. I [A 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, where R1 = H, C1-C6-alkyl, C1-C6-alkenyl, arylalkyl, R2 = R1 or alkyl, NR1R2 = a 5- or 6-membered ring, R3 = H, Me, (un)substituted aryl, C1-C6-alkyl, arylalkyl; R4 = H, C1-C6-alkyl, aryl; X, Y = (un)substituted aryl or heteroaryl] were prepd. as 5-HT<sub>2</sub> receptor antagonists. Thus, 1-(1-naphthoylamino)-3-(4-nitrophenyl)propionic acid was coupled with (S)-alanine tert-Bu ester hydrochloride using N-methylmorpholine N-oxide and EDCI in DMF to give 74% of 1-(1-naphthoylamino)-3-(4-nitrophenyl)propionylamino[propanoic acid tert-butyl ester. Procedures for prepd. of formulations contg. the title compds. are given.

RE.CN" THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RECORD FORMAT

AN : 64 CAPLUS

DIN 11

TI : .. .. . of benzazine derivatives .. .. . rhodiesterase 4 inhibitors

IN P... et ro, Mauro; Norcini, Gabriele; an i, Giancarlo; Pellacini,

Foto: Morazzoni, Gabriele; Pratielli, Lorenzo

PA 7 Group S.p.A., Italy

SO F. Int. Appl., 41 pp.

DT F 1947

LA F 1947

FAN. CH

| PI | DATE   | KIND | DATE     | 1. | ATION NO.   | DATE     |
|----|--|------|----------|----|-------------|----------|
| PI | 1947   | A1   | 20000420 | 1  | 9-EP7302    | 19991001 |
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|    | BE, CH, CY, DE, DK, ES, FR, GR, IE, IT, LU, MC, NL, SE             |      |          |    |             |          |
|    |  | B1   | 20000929 | 1  | 98-MI2216   | 19981015 |
|    |  | AA   | 20000420 | 1  | 98-MI2216   | 19981015 |
|    |  |      |          | 1  | 9-2344694   | 19991001 |
|    |  |      |          | 1  | 98-MI2216 A | 19981015 |
|    |  |      |          | 1  | 9-EP7302 W  | 19991001 |
|    |  | A1   | 20000501 | 1  | 9-63322     | 19991001 |
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|    |  |      |          | 1  | 9-EP7302 W  | 19991001 |
|    |  | A1   | 20010808 | 1  | 9-950597    | 19991001 |
|    | BE, CH, DE, DK, ES, FR, GR, IE, IT, LI, LU, NL, SE, MC, PT, SI, FI |      |          |    |             |          |
|    |  |      |          | 1  | 98-MI2216 A | 19981015 |
|    |  |      |          | 1  | 9-EP7302 W  | 19991001 |
|    | 430  | T2   | 20020821 | 2  | 9-575853    | 19991001 |
|    |  |      |          | 1  | 98-MI2216 A | 19981015 |
|    |  |      |          | 1  | 9-EP7302 W  | 19991001 |
|    | 3, 4, 5  | B1   | 20020319 | 2  | 9-806496    | 20010413 |
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OS 1947 279121

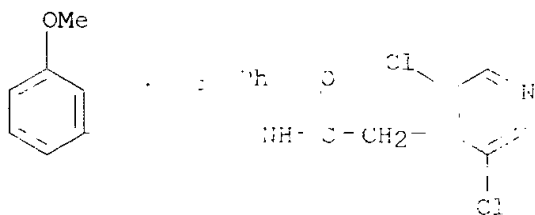
IT 274123-44-6P 264123-50-4P

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2. of benzazine derivs. as p (esterase 4 inhibitors)

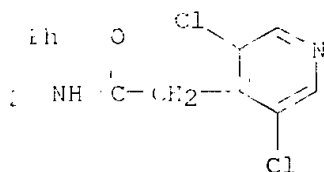
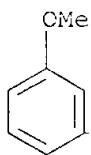
RN 2 1947 CAPLUS

CN 4 1947 acetamide, 3,5-dichloro-N-(3-ethoxyphenyl)-7-phenylheptyl]-  
(INDEX NAME)

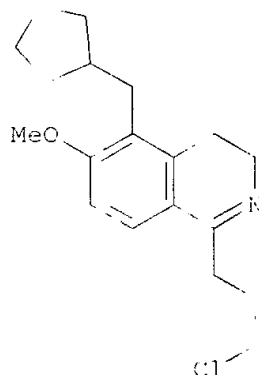
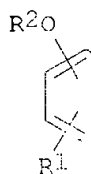


RN 1 1947 CAPLUS

CN 4 1947 acetamide, 3,5-dichloro-N-(3-ethoxyphenyl)-8-phenyloctyl]-  
(INDEX NAME)



GI



AB T. The compds. [I; A = heterocycle containing N atom and optionally unsatd. optionally further substituted by a group; R = H, CN, carbonyl, etc.; Y = CH<sub>2</sub>, (CH<sub>2</sub>)<sub>2</sub>; Z = (un)substituted aryl, heterocycle; R<sub>1</sub> = H, cycloalkyl, alkyl, etc.; R<sub>2</sub> = alkyl, polyfluoroalkyl] and the pharmaceutically acceptable salts, useful as inhibitors, were prepd. E.g., 3-step synthesis of compound II which showed IC<sub>50</sub> of 1.7 nM against PDE 4, was

RE.CN THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN REF. FORMAT

L4 7 OF 148 CAPLUS COPYRIGHT 1993

AN 2 : 1992 CAPLUS

DN

TI 1 promoted diaryl ether synthesis the construction of the F-O-G  
m of a tricyclic model

AU J. Belmont, Anthony J.; Belmont, Philip

CS of Chemistry, Case Western Reserve University, Cleveland, OH,

SO

Letters (2000), 41(11),

WILEY; ISSN: 0040-4039

PB Science Ltd.

DT

LA

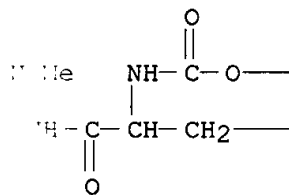
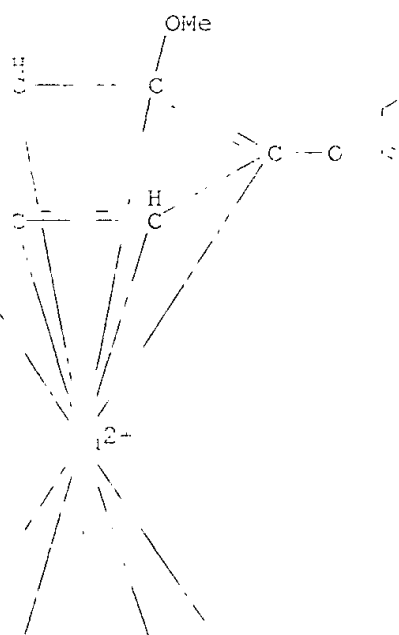
IT 272457-86-0P 272457-87-1P 272460-08-0P

I (Reactant); SPN (Synthetic product); PREP (Preparation); RACT



PAGE 1-A

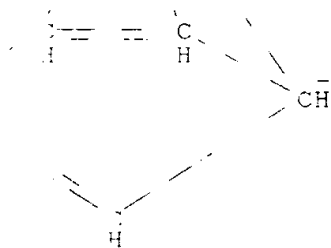
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PAGE 1-B

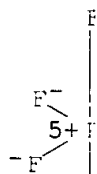
-CH<sub>2</sub>

PAGE 2-A





( 4 91-1  
( 0 . H  
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F

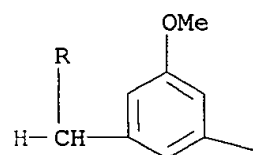
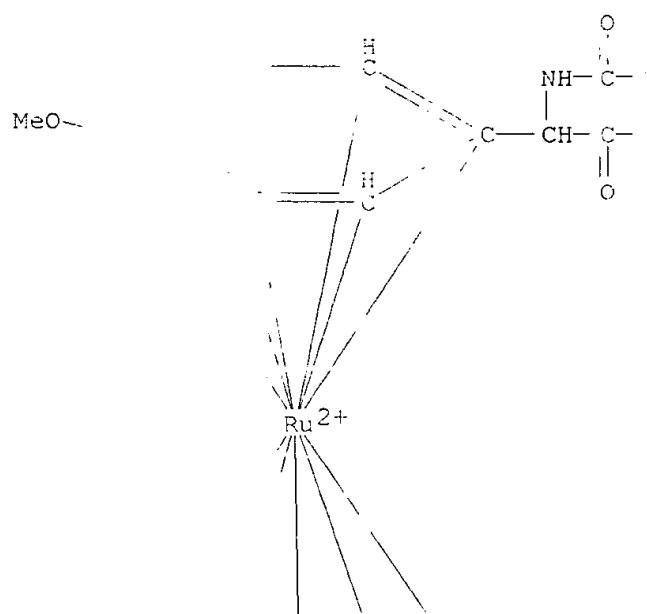
H

IT 2 162 06 7P

( synthetic preparation); PPI (action)  
( sodium-promoted diaryl ether (in the construction of the  
( ring system of teicoplanin (antibiotics)  
RN ( CAPLUS  
CN ( +), [(2S)-2-[(1,2,3,4,5,6-dichloro-4-methoxyphenyl)-N-(  
( ethylethoxy)carbonyl]glycy D-tyrosyl-(2S)-2-(3-hydroxy-  
( phenyl)-N-methylglycinamid 2,4-cyclopentadien-1-yl)-,  
( phosphate(1-) (9CI) (CA 11 11 11

( 1 -05-6  
( 116 C1 N4 O9 Ru

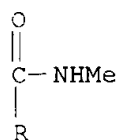
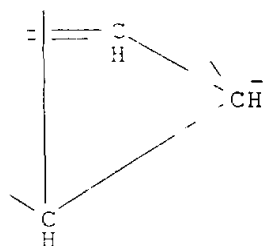
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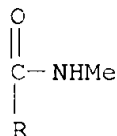
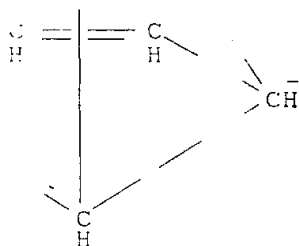
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—OH

PAGE 2-A



PAGE 2-A



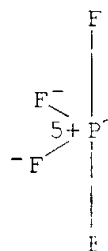
C

C

18-9

C

C



AB A n approach is described for the synthesis of glycopeptide  
 a related to teicoplanin, platinum-promoted diaryl ether  
 f followed by cycloamidation  
 RE.CNT HERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN RMAT

L4 A F 148 CAPLUS COPYRIGHT  
 AN 1 CAPLUS  
 DN 1  
 TI P on of N-(heteroaryl)ureas and serol acyltransferase  
 i  
 IN P Ernest S.  
 PA E ., USA  
 SO U ., Cont.-in-part of U. S. . 890,050, abandoned.  
 CA AM  
 DT E  
 LA 1  
 FAN.CH  
 I  
 KIND DATE  
 TION NO. DATE

Patel

5/2003&gt;

PI C A 19991214

343557 19950117

-890050 B219920528

-US3539 W 19930420

-US3539 19930420

A1 19931209

, BG, BR, CA, CZ, DE, JP,

, BE, CH, DE, DK, ES, FR,

, BJ, CF, CG, CI, CM, GA,

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, IT, LU, MC, NL, PT, SE,

, NE, SN, TD, TG

890050 A219920528

# PATENT INFORMATION:

FAN

KIND DATE

ION NO. DATE

PI W A1 19931209

US3539 19930420

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, RO, RU, SK, UA, US

, IT, LU, MC, NL, PT, SE,

, NE, SN, TD, TG

890050 A219920528

A1 19931230

-40283 19930420

-890050 A 19920528

-US3539 A 19930420

-909519 19930420

A1 19950315

, BE, CH, DE, DK, ES, FR,

, IT, LI, LU, NL, PT, SE

890050 A 19920528

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T2 19950420

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-890050 A 19920528

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C 19970701

-2134359 19930420

-890050 A 19920528

A 19980915

-6421 19930420

-890050 A 19920528

US3539 W 19930420

A2 9931228

1552 19930527

890050 A 19920528

A 9910119

106774 19930527

890050 A 19920528

A 19941125

-4530 19941125

-890050 A 19920528

-US3539 A 19930420

A 19991214

-343557 19950117

-890050 B219920528

US3539 W 19930420

OS 22878

IT 1 12-OP

Biological activity or effe

Classified); SIN (Synthetic

Medical study; PREP (Prep

of N-(heteroaryl)ureas a

ols)

pt adverse); BSU (Biological

on); THU (Therapeutic use);

USES (Uses)

rol acyltransferase

RN CAPLUS

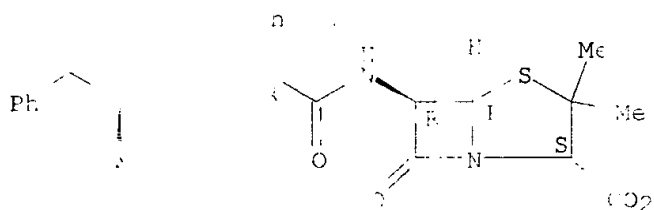
CM 4-bis(ethylthio)-6-methy

nyl)-6-phenylhexyl]- (9CI

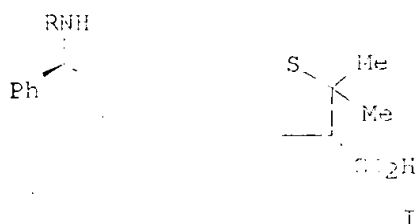
nyl]-N'-[2-(2,5-

DEX NAME)



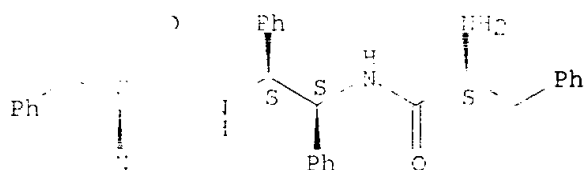


GI



|      |   |  |
|------|---|--|
| AE   | [R = COCH <sub>2</sub> NH <sub>2</sub> , COCH <sub>2</sub> Me], CH(NH <sub>2</sub> )CH <sub>2</sub> Ph-(S), |  |
|      | (S), COCH <sub>2</sub> NHCOCCH <sub>2</sub> NH <sub>2</sub> ; .1 -  | -4-yl] were prepd. from                              |
|      | and a series of amino ac.   | -Gly, N-Boc-Ala, N-Boc-Phe,                          |
|      | and a peptide, glycylgly-   | were tested for their                                |
|      | stability and antibacter  | : [I {R = COCH(NH <sub>2</sub> )CH <sub>2</sub> Ph}, |
|      | .g/mL vs. S. aureus and   | vs. E. coli ].                                       |
| RECN | HERE ARE 8 CITED REFERENCES   | FOR THIS RECORD                                      |
|      | CITATIONS AVAILABLE IN  | SMAT   |
| L4   | P 148 CAPLIN'S COPYRIGHT  |  |
| AN   | CAPLIN  |  |
| DN   |   |  |
| TI   | and supported copper com  | cyclic and open-chain                                |
|      | nated ligands as catalyst   | propanation reactions                                |
| AU   | Burguete, M. I.; Fraile,  | Garcia, J. I.; Garcia, J.;                           |
|      | na, Enrique; Luis, S. V.;   | J. A.; Royo, A. J.; Sanchez,                         |
| CS   | Inorganica, Un  | I, Castellon, E-12080, Spain                         |
| SO   | Journal of Inorganic Chemis   | , (12), 2347-2354                                    |
|      | CO; ISSN: 1134-1948   |  |
| PE   | erlag GmbH  |  |
| DT   |   |  |
| LA   |   |  |
| IT   | 2 2416 22-5P 253426-93-6P   |  |
|      | catalyst use); SPN (Synthe  | tion); PREP (Preparation);                           |
|      | of cyclic and open-chain  | nated ligands and the                                |
|      | of thior Cu(I) and Cu(II)   | s as homogeneous and                                 |
|      | d catalysts of cycloprope   | ctions)  |
| RN   | CAPLIN  |  |
| CN   | named H <sub>2</sub> O-{(1S,2S-1,1,1-tri-2-ethanediyl)b   | 1,1,1-tri-2-ethanediyl}bis[.alpha.-                  |
|      | pha.S...].a.'S)- (S,1)  | NAME)  |

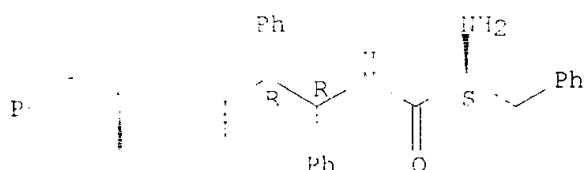
Absolu te chemistry. Rotation (-).



RM 2 6- CAPITE

CN B ne rranamide, N,N'-[(1R,2R)-1,2-ethanediyl]bis[.alpha.-  
and -, (.alpha.S,.alpha.'S)- (9CI) (X NAME)

Absolu te chemistry. Rotation (-).



AB 1. Cu(II) complexes of cyclic chain polyaza compds. were  
used as catalysts in the benchmark penation reaction of styrene  
with acetoacetate. In general, the amts. of Cu are needed to  
promote the reaction. The catalytic activity depends on the structure of  
the ligand, e.g. amine amides are more effective than polyamines, and on  
the state of Cu, Cu(II) being more effective than Cu(I). Given that  
Cu(II) is the active species, these results must be related to  
the properties of the complexes. The behavior of the counterion also has a  
marked influence on the catalytic activity, the role of which is  
under study. XAS measurements suggest the formation of oligomeric species.  
The chiral ligands lead to enantiomeric excesses.  
The ligands can easily be supported on org. polymers and their  
use can be used as catalysts. In the case of cyclic and acyclic  
ligands, they can be supported on clays and the solids  
tend to promote the reaction and decrease in the trans/cis

RELCNT THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN REAT

L4 1 R 3 OF 148 APINE COPYRIGHT

AN 1 3 OF 148 CAPITE

DN 1 3 OF 148

TI 1 3 OF 148 of .alpha.-. toamide poly as antiviral HCV proteinase

IN 1 3 OF 148 Nigella; John, Philip; Paul Brittain; Raynham,

EL 1 3 OF 148 Wilson, Francis Xavier

PL 1 3 OF 148 La Roche A. L., Switzer.

SI 1 3 OF 148 130 op.

DT 1 3 OF 148

LA 1 3 OF 148

FAH.CN 1 3 OF 148

KIND DATE

NO. DATE

• 24 •

C. 32:43653

Biological activity or effect; (Synthetic)  
Biological study; REP (Protein)  
of alpha-amide peptides

CN      - amide, N-3-(acryloyl)-1-oxypropanoic acid  
-O-methyl 1-hydroxy-2-propylalanyl- (L-alanine)  
-acetyl)propyl- (BACI) (BACI)

```

,      ert adverse); BSU (Biological
p      on); THU (Therapeutic use);
o      ES (Uses)
c      vidual HCV proteinase

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```

-1      .aspartyl-L-.alpha.-
pl      .acyl-N-[(1S)-1-
X

```

Ans:                schemis. y.



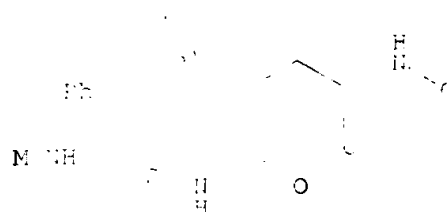
2003>





0-2-4-

200



AB 1 agent, contain matrix metallopro- tors, TNF- $\alpha$ .-  
2 rting enzyme inhibi rs, and/ solubilization inhibitors  
3 n ingredients. he agents. ase in bone marrow cells  
4 opnosis. [4- hydroxyanth entyl-3(S)-methylsuccinyl]-  
5 onyl pyridine-1-methyl ide (I) in to ptosis of nucleated bone  
6 e to be sampled f myelodyspl to these patients.  
7 acutical patients. trol. or were also given.

L. 35 OF 148 CAPLW COPYRIGHT

A' : 50 and CAPL'S

DE: 45-61

Titration of an aqueous solution of phenol containing compounds and  
determination of novel and specific inhibitors

Aff. Gustave; Gill, Carla L.; Michael D.; Blanchard,

L.; Guse, Father V.; Epstein, ...; Pal, Kollol

So. J. Med. & Medical Chemistry 1919, 9(19), 2849-2854

LF3; I. N. 01 024X

Physics

D 11

IR 2 32-54-6P

... (Biological) ... (Synthetic) ... BIOL (Biological)

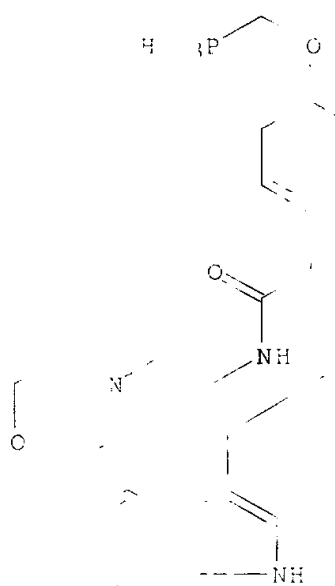
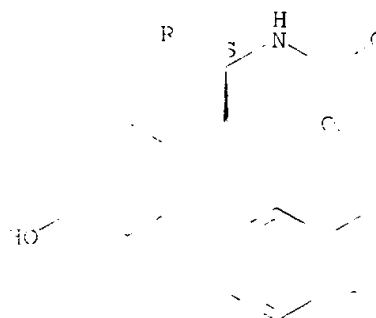
using the coordinate library of dipeptidyl phosphatase to identify the fragments of Cdc25

RECEIVED 1966 CAP...

Chemical name: N-(4-Hydroxyphenyl)-n-9-ylmethyl-L-tyrosyl-N2-[2-(1H-

1-ethyl-4-(2-morpholinoethoxy)benzene (9CI)

Absol: to chemist.



A: Four or more "ligation was rep. a library of  
 identified compounds. In order to express the requirements of the key  
 of the phosphatase, bc25. Several surrogates were  
 reported as in the U. product of the mono- or  
 phosphatase substrate.  
 REFERENCE: HERE ARE 22 REFERENCES FOR THIS RECORD  
 THE CITATIONS AVAILABLE TO THE

LA 148 EXPLU COPYRIGHT  
AP 6396 CAP  
DP 63174

T... culture activities; relationship of ...  
... bond ... and TMT-...  
At ... , Honorable Hayashi, Ryodoh ...  
... ; ... , ... ; ...

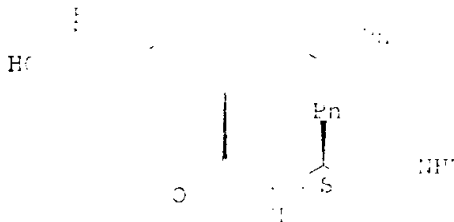
sed inhibitors on  
ing  
shi; Yoshino, Koichiro;  
ko; Yagita, Hideo;

C. I. Murakami, National Research Institute for Chemical Process, 1-1-4 Higashi, Suita, Osaka, 534-8666, Japan  
S. I. Murakami, National Research Institute for Chemical Process, 1-1-4 Higashi, Suita, Osaka, 534-8666, Japan  
C. I. Murakami, National Research Institute for Chemical Process, 1-1-4 Higashi, Suita, Osaka, 534-8666, Japan  
P. I. Murakami, National Research Institute for Chemical Process, 1-1-4 Higashi, Suita, Osaka, 534-8666, Japan  
D. I. Murakami, National Research Institute for Chemical Process, 1-1-4 Higashi, Suita, Osaka, 534-8666, Japan  
L. I. Murakami, National Research Institute for Chemical Process, 1-1-4 Higashi, Suita, Osaka, 534-8666, Japan

IN 1 728-61-2P 188728-67--  
 1 Fluoride toxicity or effect; adverse); BSU (Biological  
 1 Synthesis; (Synthetic) ; THU (Therapeutic use);  
 1 Biological study REP (Preparation) (Uses)  
 1 Inhibitors on e-based inhibitors on  
 1 Mechanism of action and T... (Processing)

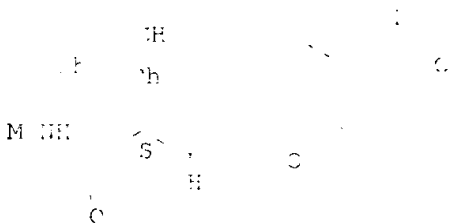
RX 1 128- CARBON  
 CH E amoc e, H (R) N1-[(1-2 th -2-oxo-1-phenylethyl)-2-  
 ber (1)- (R) (I) N

As per ...



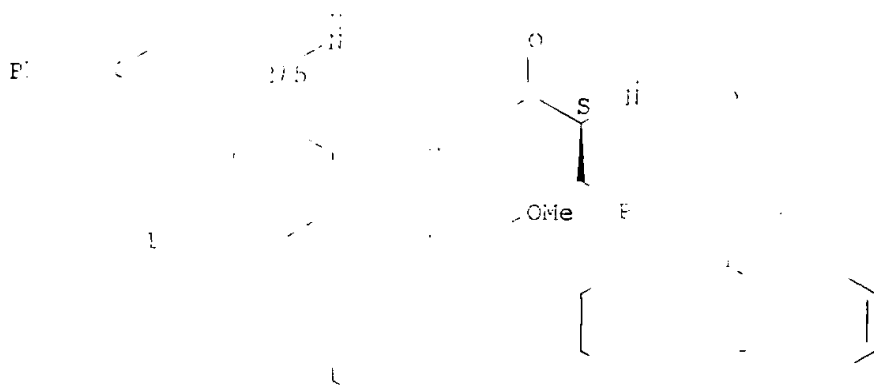
Chemical name: N-ethyl-N-(2-oxo-1-phenylethyl)-2-phenylacetamide

Also see miss.

[illegible]

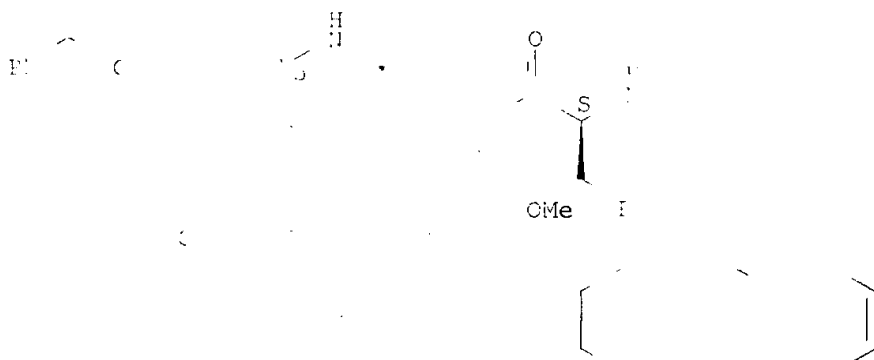


Q



RI 142 24 CAPL  
 Cl 142 24 CAPL  
 3-ylmeth  
 -[[6-ox  
 hyl ester  
 en. -L-phenylalanyl-3-  
 (noxy)hexyl]amino]-1-(4-  
 INDEX NAME)

Ab 142 24 CAPL



G

R<sup>5</sup>  
 R N

I

P

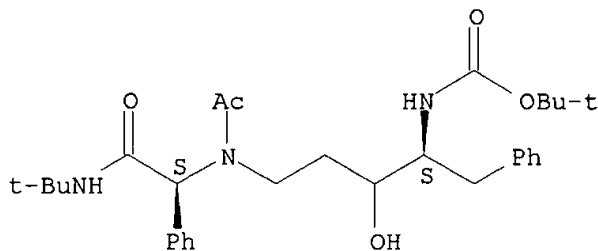
'2003>

AB Title compds. [I; R1 = cycloalkyl or aralkyl; R2 = cycloalkylmethyl or (ar)alkyl; R3 = H, F, alkyl, substituted Ph; R4 = H, alkyl, acyl, substituted Ph; R5 = H; R1R5 = atoms to complete a ring] were prepd. Thus, L-R2CH(NH2)CO2Me.HCl (R2 = cyclohexyl), 4-(NC)C6H4CHO, N-Fmoc-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid, and 4-(CNH2CH2C)C6H4OCH2Ph were subjected to Ugi condensation and the product cyclized to give, after deprotection, I [R1R5 = 2-(H2C)C6H4CH2, R2 = cyclohexylmethyl, R3 = 4-(NC)C6H4, R4 = CH2CH2C6H4(OH)-4]. Data for biol. activity of I were given.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

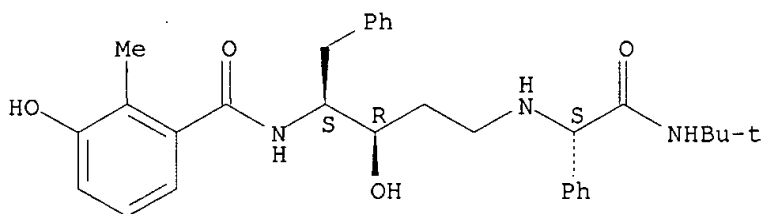
L4 ANSWER 38 OF 148 CAPLUS COPYRIGHT 2003 ACS  
AN 1999:581403 CAPLUS  
DN 132:106  
TI Design and synthesis of a novel series of HIV-1 protease inhibitors  
AU Takashiro, E.; Nakamura, Y.; Miyamoto, S.; Ozawa, Y.; Sugiyama, A.; Fujimoto, K.  
CS Exploratory Chemistry Research Laboratories, Sankyo Co. Ltd., Tokyo, Japan  
SO Bioorganic & Medicinal Chemistry (1999), 7(9), 2105-2114  
CODEN: BMECEP; ISSN: 0968-0896  
PB Elsevier Science Ltd.  
DT Journal  
LA English  
OS CASREACT 132:106  
IT **251339-75-0P 251339-81-8P 251339-82-9P**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(design and synthesis of a novel series of HIV-1 protease inhibitors and structure-activity relations)  
RN 251339-75-0 CAPLUS  
CN D-glycero-Pentitol, 5-[acetyl[(1S)-2-[(1,1-dimethylethyl)amino]-2-oxo-1-phenylethyl]amino]-1,2,4,5-tetradexo-2-[[[(1,1-dimethylethoxy)carbonyl]amino]-1-phenyl]-, (3.xi.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 251339-81-8 CAPLUS  
CN D-erythro-Pentitol, 1,2,4,5-tetradexo-5-[[[(1S)-2-[(1,1-dimethylethyl)amino]-2-oxo-1-phenylethyl]amino]-2-[(3-hydroxy-2-methylbenzoyl)amino]-1-phenyl]- (9CI) (CA INDEX NAME)

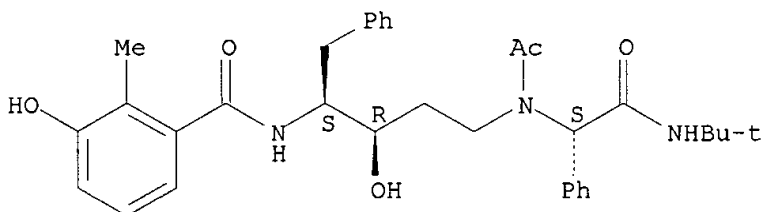
Absolute stereochemistry.



RN 251339-82-9 CAPLUS

CN D-erythro-Pentitol, 5-[acetyl[(1S)-2-[(1,1-dimethylethyl)amino]-2-oxo-1-phenylethyl]amino]-1,2,4,5-tetradexo-2-[(3-hydroxy-2-methylbenzoyl)amino]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The synthesis and the SAR study of novel pseudo sym. inhibitors of HIV-1 protease are described. Michael addn. of amino acid derivs. to vinyl ketones was utilized to derive a potent (nM) series of HIV-1 protease inhibitors.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 39 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1999:569665 CAPLUS

DN 131:310411

TI Samarium-induced iodine-catalyzed reduction of imines: synthesis of amine derivatives

AU Banik, Bimal K.; Zegrocka, Oliwia; Banik, Indrani; Hackfeld, Linda; Becker, Frederick F.

CS M.D. Anderson Cancer Center, Department of Molecular Pathology, Section of Experimental Pathology, The University of Texas, Houston, TX, 77030, USA

SO Tetrahedron Letters (1999), 40(37), 6731-6734

CODEN: TELEAY; ISSN: 0040-4039

PB Elsevier Science Ltd.

DT Journal

LA English

OS CASREACT 131:310411

IT 247909-18-8P

RL: SPN (Synthetic preparation); PREP (Preparation)

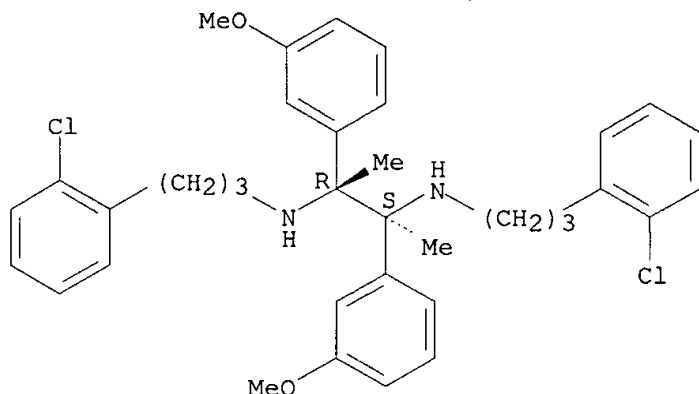
(samarium-induced iodine-catalyzed redn. of imines derived from arom. amines to secondary monoamines and reductive dimerization of imines derived from arylalkyl amines to secondary diamines)

RN 247909-18-8 CAPLUS

CN 2,3-Butanediamine, N,N'-bis[3-(2-chlorophenyl)propyl]-2,3-bis(3-methoxyphenyl)-, (2R,3S)-rel- (9CI) (CA INDEX NAME)



Relative stereochemistry.



AB Samarium metal induced iodine-catalyzed redn. of the imines to secondary amines was investigated. The imines derived from arom. amines produced monoamines whereas imines from arylalkyl amines gave diamines in good yield.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 40 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1999:457798 CAPLUS

DN 131:228963

TI Reductive ring cleavage of 1-alkyl-4-benzoylamino-5-phenyl-3-pyrazolidinones with raney-nickel alloy. Synthesis of N-benzoyl-3-alkylamino-3-phenylalanine amides from rel-(4R,5R)-4-benzoylamino-5-phenyl-3-pyrazolidinone

AU Zupancic, Silvo; Svete, Jurij; Stanovnik, Branko

CS Faculty of Chemistry and Chemical Technology, University of Ljubljana, Ljubljana, 1000, Slovenia

SO Journal of Heterocyclic Chemistry (1999), 36(3), 607-610  
CODEN: JHTCAD; ISSN: 0022-152X

PB HeteroCorporation

DT Journal

LA English

OS CASREACT 131:228963

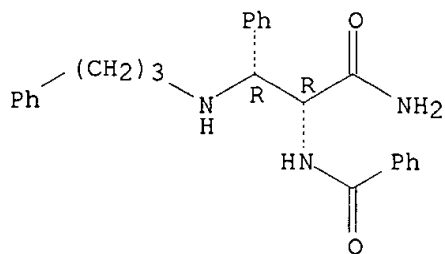
IT **243842-79-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(reductive ring cleavage of alkylated pyrazolidinones with raney-nickel alloy in synthesis of amino acids amides)

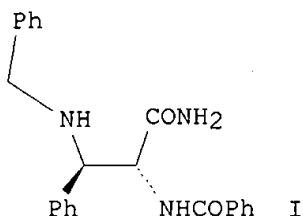
RN 243842-79-7 CAPLUS

CN Benzenepropanamide, .alpha.-(benzoylamino)-.beta.-[(3-phenylpropyl)amino]-, (.alpha.R,.beta.R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



GI



AB Rel-(4R,5R)-4-Benzoylamino-5-phenyl-3-pyrazolidinone was alkylated at position 1 with carbonyl compds. The corresponding rel-(4R,5R)-4-benzoylamino-5-phenyl-3-pyrazolidinone-1-azomethine imines were treated with sodium borohydride to give rel-(4R,5R)-1-alkyl-4-benzoylamino-5-phenyl-3-pyrazolidinones. Redn. of pyrazolidinones with Raney-nickel alloy in methanolic potassium hydroxide furnished rel-(4R,5R)-N-benzoyl-3-alkylamino-3-phenylalanine amides, e.g. I.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 41 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1999:292590 CAPLUS

DN 130:338021

TI Preparation of arylacetic amide derivatives as a preventive or remedy for urinary disorders

IN Kaihoh, Terumitsu; Okada, Tomomi; Takahashi, Yoshinori; Mizuno, Hiroyuki; Honda, Haruyoshi; Sato, Susumo

PA SSP Co., Ltd., Japan

SO Eur. Pat. Appl., 21 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.  | DATE     |
|----|---|------|----------|------------------|----------|
| PI | EP 913393   | A2   | 19990506 | EP 1998-120422   | 19981028 |
|    | EP 913393   | A3   | 19990526 |                  |          |
|    | EP 913393   | B1   | 20030212 |                  |          |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO |      |          |                  |          |
|    |   |      |          | JP 1997-300352 A | 19971031 |
|    | JP 11193271   | A2   | 19990721 | JP 1998-290576   | 19981013 |

|            |   |          |                           |
|------------|---|----------|---------------------------|
| US 6060485 | A | 20000509 | JP 1997-300352 A 19971031 |
|            |   |          | US 1998-181091 19981028   |
| CN 1222510 | A | 19990714 | JP 1997-300352 A 19971031 |
|            |   |          | CN 1998-122655 19981030   |
| TW 442470  | B | 20010623 | JP 1997-300352 A 19971031 |
|            |   |          | TW 1998-87118071 19981030 |
|            |   |          | JP 1997-300352 A 19971031 |

OS MARPAT 130:338021

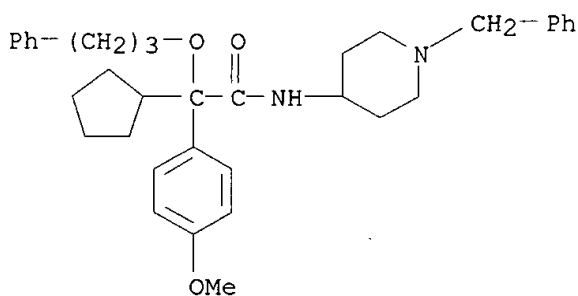
IT **224034-69-9P 224034-79-1P 224034-80-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of arylacetic amide derivs. as a preventive or remedy for urinary disorders)

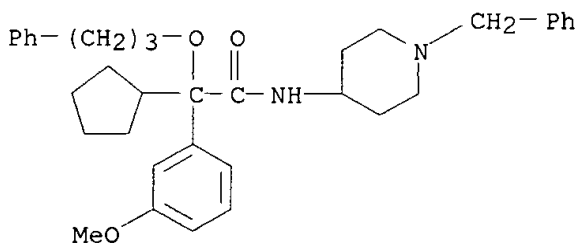
RN 224034-69-9 CAPLUS

CN Benzeneacetamide, .alpha.-cyclopentyl-4-methoxy-N-[1-(phenylmethyl)-4-piperidiny]-.alpha.-(3-phenylpropoxy)- (9CI) (CA INDEX NAME)



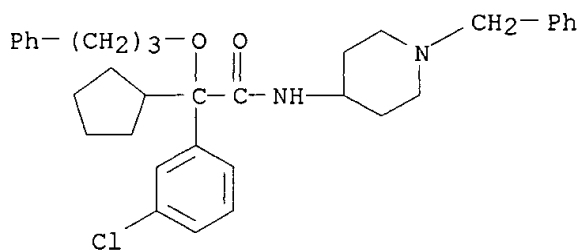
RN 224034-79-1 CAPLUS

CN Benzeneacetamide, .alpha.-cyclopentyl-3-methoxy-N-[1-(phenylmethyl)-4-piperidiny]-.alpha.-(3-phenylpropoxy)- (9CI) (CA INDEX NAME)

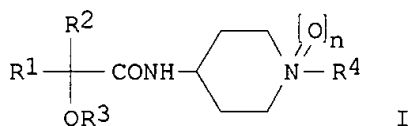


RN 224034-80-4 CAPLUS

CN Benzeneacetamide, 3-chloro-.alpha.-cyclopentyl-N-[1-(phenylmethyl)-4-piperidiny]-.alpha.-(3-phenylpropoxy)- (9CI) (CA INDEX NAME)



GI



AB The title compds. [I; R1 = (un)substituted arom. hydrocarbon or heteroarom. group; R2, R3 = (un)substituted hydrocarbon or heterocyclic group; R4 = H, (un)substituted hydrocarbon or heterocyclic group; n = 0-1] and their salts which have both excellent anticholinergic action and calcium antagonism and at the same time have high selectivity to bladder, so that they are useful as preventives or remedies for urinary disorders, were prepd. Thus, treatment of N-(1-benzyl-4-piperidiny)-2-hydroxy-3-methyl-2-phenylbutanamide with NaH in DMF followed by addn. of BuI and a soln. of Bu4NI in DMF afforded 28% I [R1 = Ph; R2 = iPr; R3 = Bu; R4 = PhCH2; n = 0] which showed ID50 of 9.8 mg/kg against bladder contraction in rats.

L4 ANSWER 42 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1999:281303 CAPLUS

DN 131:130143

TI Enantioselective synthesis of the chroman moiety of vitamin E

AU Tietze, Lutz F.; Gorlitzer, Jochen; Schuffenhauer, Ansgar; Hubner, Matthias

CS Institute Organic Chemistry, Georg-August-Univ., Gottingen, D-37077, Germany

SO European Journal of Organic Chemistry (1999), (5), 1075-1084

CODEN: EJOCFK; ISSN: 1434-193X

PB Wiley-VCH Verlag GmbH

DT Journal

LA English

OS CASREACT 131:130143

IT **197297-78-2P**

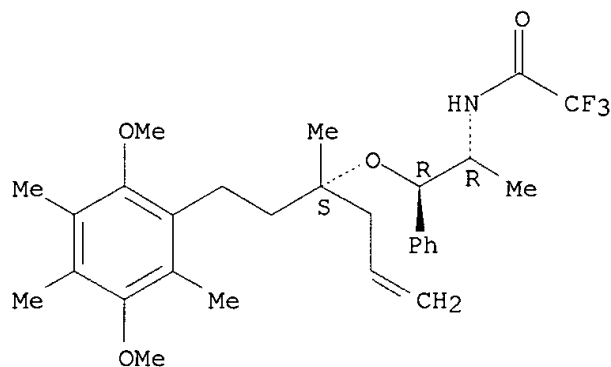
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(enantioselective synthesis of chroman moiety of vitamin E)

RN 197297-78-2 CAPLUS

CN Acetamide, N-[(1R,2R)-2-[[[(1S)-1-[2-(2,5-dimethoxy-3,4,6-trimethylphenyl)ethyl]-1-methyl-3-butenyl]oxy]-1-methyl-2-phenylethyl]-2,2,2-trifluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



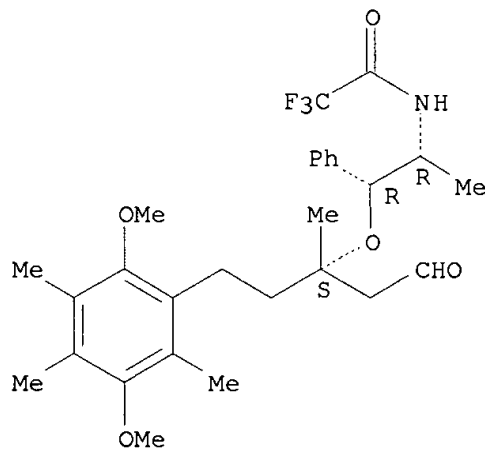
IT 197297-80-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(enantioselective synthesis of chroman moiety of vitamin E)

RN 197297-80-6 CAPLUS

CN Acetamide, N-[(1R,2R)-2-[(S)-1-[2-(2,5-dimethoxy-3,4,6-trimethylphenyl)ethyl]-1-methyl-3-oxopropoxy]-1-methyl-2-phenylethyl]-2,2,2-trifluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB Several approaches for the enantioselective synthesis of the chroman moiety of .alpha.-tocopherol are described.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 43 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1999:139868 CAPLUS

DN 130:196958

TI Preparation of 3-tert-butyl-L-tyrosinamide-containing peptides and related compounds exhibiting a motilin receptor antagonism

IN Kotake, Ken-ichiro; Kozono, Toshiro; Sato, Tsutomu; Takanashi, Hisanori

PA Chugai Seiyaku Kabushiki Kaisha, Japan

SO PCT Int. Appl., 144 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO.  | DATE     |
|----|--|------|----------|------------------|----------|
| PI | WO 9909053   | A1   | 19990225 | WO 1998-JP3627   | 19980814 |
|    | W:   |      |          |                  |          |
|    | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                  |          |
|    | RW:  |      |          |                  |          |
|    | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |      |          |                  |          |
|    |  |      |          | JP 1997-255879 A | 19970815 |
|    |  |      |          | JP 1998-186802 A | 19980528 |
|    | TW 460478  | B    | 20011021 | TW 1998-87113211 | 19980811 |
|    |  |      |          | JP 1997-255879 A | 19970815 |
|    |  |      |          | JP 1998-186802 A | 19980528 |
|    | CA 2301687   | AA   | 19990225 | CA 1998-2301687  | 19980814 |
|    |  |      |          | JP 1997-255879 A | 19970815 |
|    |  |      |          | JP 1998-186802 A | 19980528 |
|    |  |      |          | WO 1998-JP3627 W | 19980814 |
|    | AU 9886490   | A1   | 19990308 | AU 1998-86490    | 19980814 |
|    | AU 741216  | B2   | 20011129 |                  |          |
|    |  |      |          | JP 1997-255879 A | 19970815 |
|    |  |      |          | JP 1998-186802 A | 19980528 |
|    |  |      |          | WO 1998-JP3627 W | 19980814 |
|    | JP 2000044595  | A2   | 20000215 | JP 1998-229586   | 19980814 |
|    |  |      |          | JP 1997-255879 A | 19970815 |
|    |  |      |          | JP 1998-186802 A | 19980528 |
|    | EP 1006122   | A1   | 20000607 | EP 1998-937826   | 19980814 |
|    | R:   |      |          |                  |          |
|    | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI   |      |          |                  |          |
|    |  |      |          | JP 1997-255879 A | 19970815 |
|    |  |      |          | JP 1998-186802 A | 19980528 |
|    |  |      |          | WO 1998-JP3627 W | 19980814 |
|    | US 6255285   | B1   | 20010703 | US 2000-485620   | 20000215 |
|    |  |      |          | JP 1997-255879 A | 19970815 |
|    |  |      |          | JP 1998-186802 A | 19980528 |
|    |  |      |          | WO 1998-JP3627 W | 19980814 |
| OS | MARPAT 130:196958  |      |          |                  |          |
| IT | 220806-34-8P 220806-55-3P 220806-57-5P   |      |          |                  |          |
|    | 220807-12-5P 220807-14-7P 220807-18-1P   |      |          |                  |          |
|    | 220807-21-6P 220807-23-8P 220807-24-9P   |      |          |                  |          |
|    | 220807-34-1P 220807-43-2P 220807-92-1P   |      |          |                  |          |
|    | 220807-93-2P 220807-98-7P 220807-99-8P   |      |          |                  |          |
|    | 220808-00-4P 220808-11-7P 220808-24-2P   |      |          |                  |          |
|    | 220808-25-3P   |      |          |                  |          |
|    | RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  |      |          |                  |          |
|    | (prepn. of 3-tert-butyl-L-tyrosinamide-contg. peptide compds. as motilin receptor antagonists, inhibitors of digestive tract motility, and remedy for high blood motilin)  |      |          |                  |          |
| RN | 220806-34-8 CAPLUS   |      |          |                  |          |

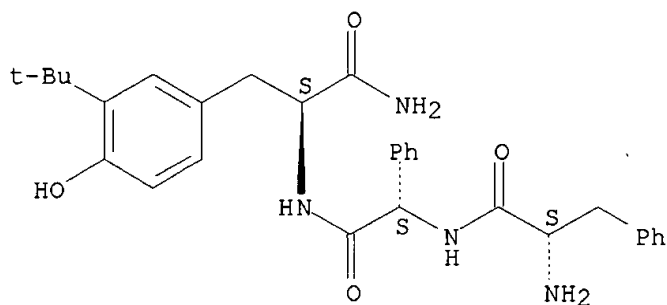
CN L-Tyrosinamide, L-phenylalanyl-(2S)-2-phenylglycyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-33-7

CMF C30 H36 N4 O4

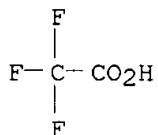
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 220806-55-3 CAPLUS

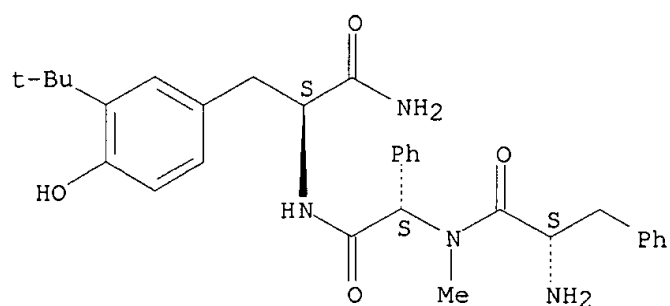
CN L-Tyrosinamide, L-phenylalanyl-(2S)-N-methyl-2-phenylglycyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-54-2

CMF C31 H38 N4 O4

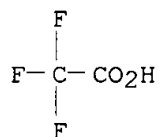
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 220806-57-5 CAPLUS

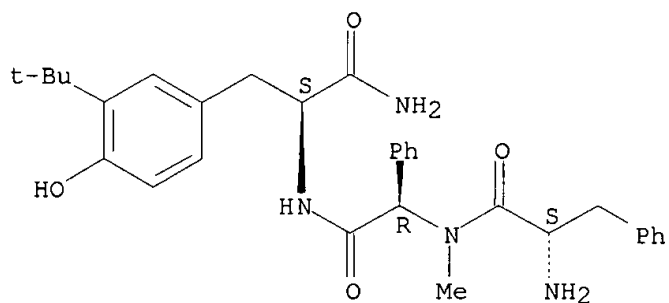
CN L-Tyrosinamide, L-phenylalanyl-(2R)-N-methyl-2-phenylglycyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-56-4

CMF C31 H38 N4 O4

Absolute stereochemistry.

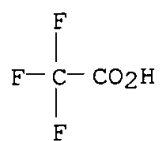


CM 2

CRN 76-05-1

CMF C2 H F3 O2

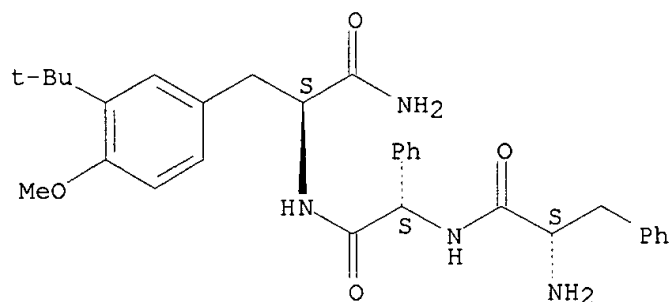




RN 220807-12-5 CAPLUS

CN L-Tyrosinamide, L-phenylalanyl-(2S)-2-phenylglycyl-3-(1,1-dimethylethyl)-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220807-14-7 CAPLUS

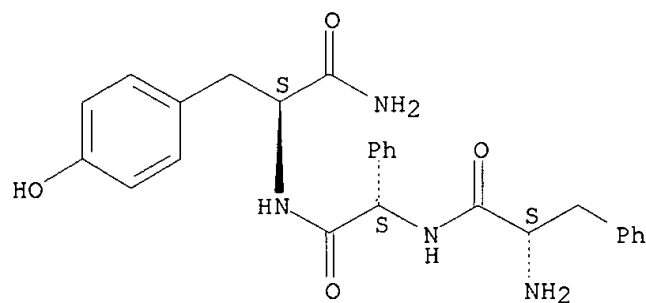
CN L-Tyrosinamide, L-phenylalanyl-(2S)-2-phenylglycyl-,  
mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220807-13-6

CMF C26 H28 N4 O4

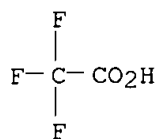
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 220807-18-1 CAPLUS

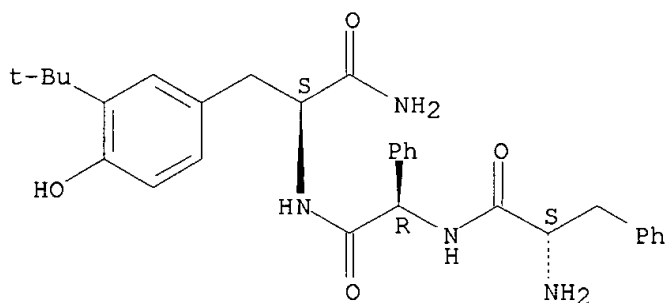
CN L-Tyrosinamide, L-phenylalanyl-(2R)-2-phenylglycyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220807-17-0

CMF C30 H36 N4 O4

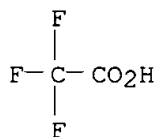
Absolute stereochemistry.



CM 2

CRN 76-05-1

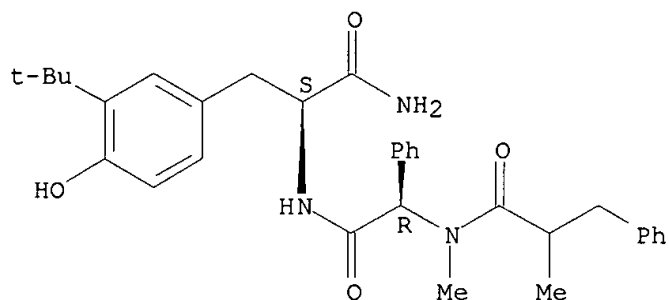
CMF C2 H F3 O2



RN 220807-21-6 CAPLUS

CN L-Tyrosinamide, (2R)-N-methyl-N-(2-methyl-1-oxo-3-phenylpropyl)-2-phenylglycyl-3-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

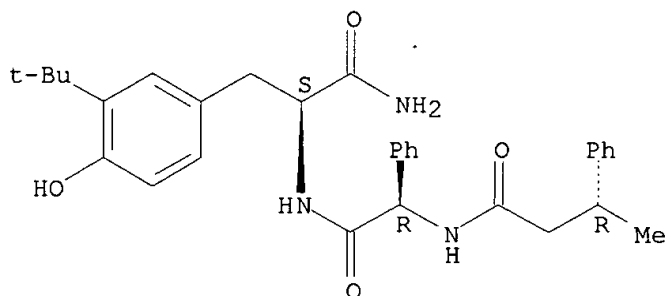
Absolute stereochemistry.



RN 220807-23-8 CAPLUS

CN L-Tyrosinamide, (2R)-N-[(3R)-1-oxo-3-phenylbutyl]-2-phenylglycyl-3-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

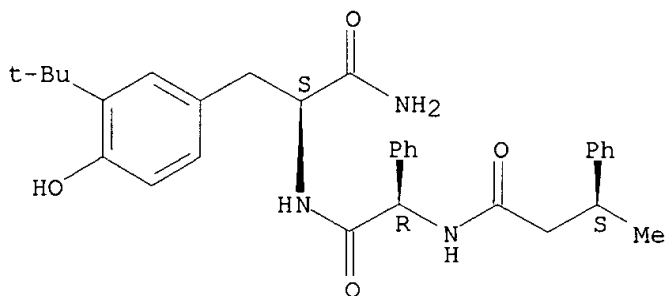
Absolute stereochemistry.



RN 220807-24-9 CAPLUS

CN L-Tyrosinamide, (2R)-N-[(3S)-1-oxo-3-phenylbutyl]-2-phenylglycyl-3-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220807-34-1 CAPLUS

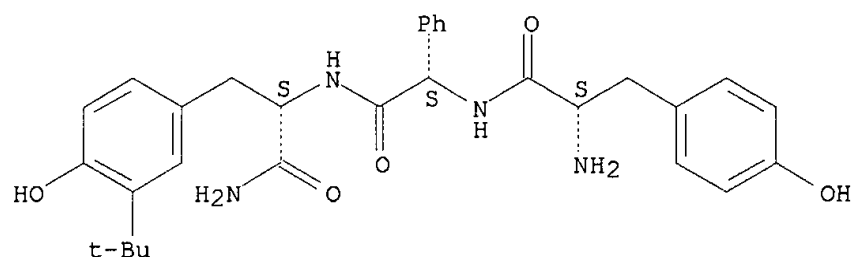
CN L-Tyrosinamide, L-tyrosyl-(2S)-2-phenylglycyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220807-33-0

CMF C30 H36 N4 O5

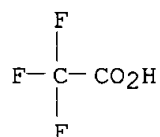
Absolute stereochemistry.



CM 2

CRN 76-05-1

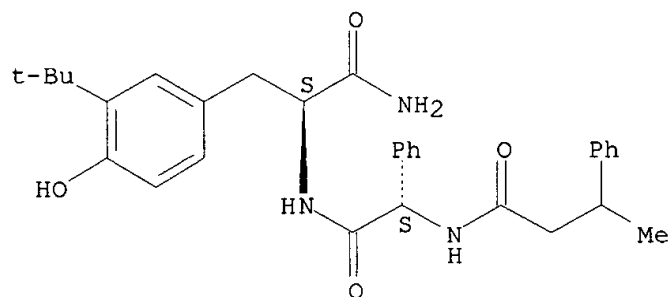
CMF C2 H F3 O2



RN 220807-43-2 CAPLUS

CN L-Tyrosinamide, (2S)-N-(1-oxo-3-phenylbutyl)-2-phenylglycyl-3-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220807-92-1 CAPLUS

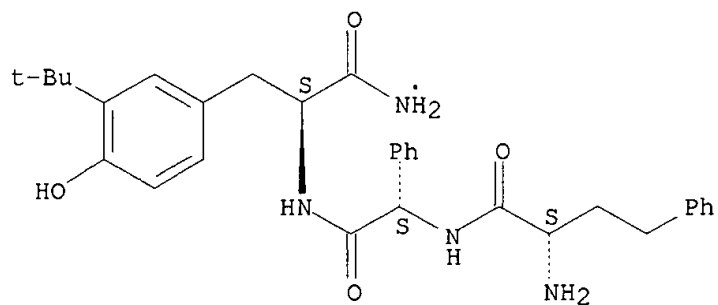
CN L-Tyrosinamide, (.alpha.S)-.alpha.-aminobenzenebutanoyl-(2S)-2-phenylglycyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220807-91-0

CMF C31 H38 N4 O4

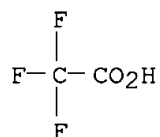
Absolute stereochemistry.



CM 2

CRN 76-05-1

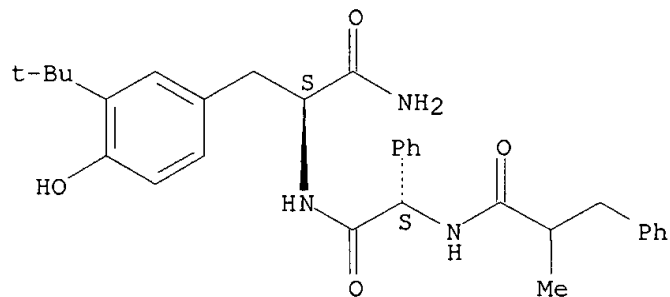
CMF C2 H F3 O2



RN 220807-93-2 CAPLUS

CN L-Tyrosinamide, (2S)-N-(2-methyl-1-oxo-3-phenylpropyl)-2-phenylglycyl-3-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

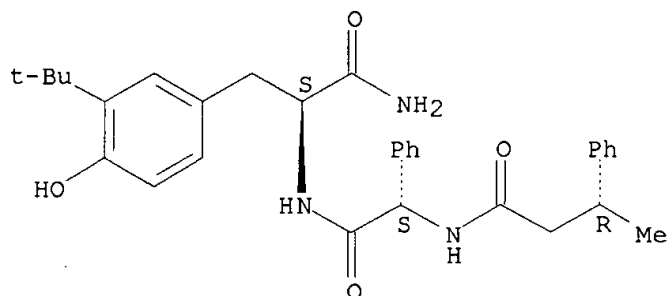
Absolute stereochemistry.



RN 220807-98-7 CAPLUS

CN L-Tyrosinamide, (2S)-N-[(3R)-1-oxo-3-phenylbutyl]-2-phenylglycyl-3-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

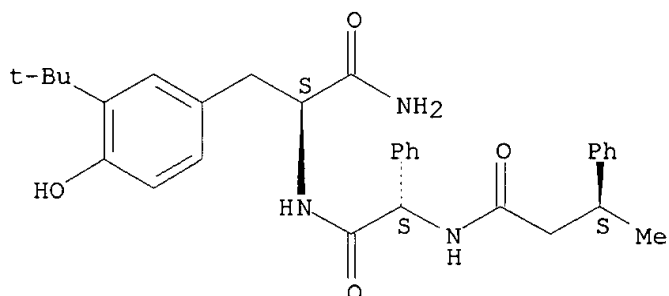
Absolute stereochemistry.



RN 220807-99-8 CAPLUS

CN L-Tyrosinamide, (2S)-N-[(3S)-1-oxo-3-phenylbutyl]-2-phenylglycyl-3-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

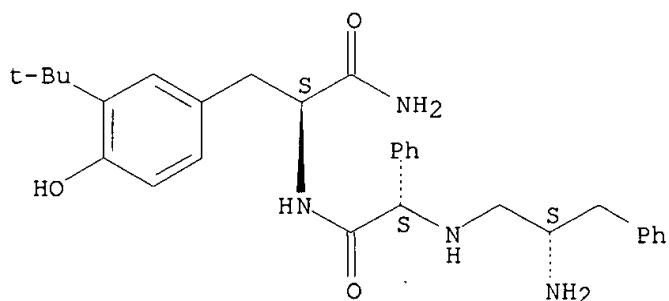
Absolute stereochemistry.



RN 220808-00-4 CAPLUS

CN L-Tyrosinamide, (2S)-N-[(2S)-2-amino-3-phenylpropyl]-2-phenylglycyl-3-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

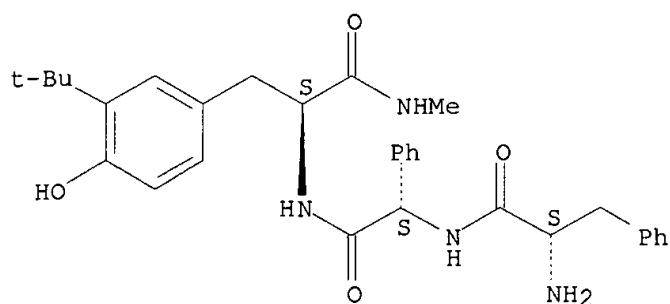
Absolute stereochemistry.



RN 220808-11-7 CAPLUS

CN L-Tyrosinamide, L-phenylalanyl-(2S)-2-phenylglycyl-3-(1,1-dimethylethyl)-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220808-24-2 CAPLUS

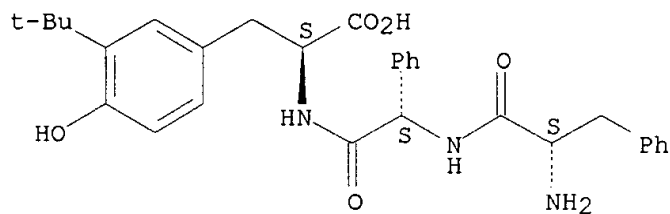
CN L-Tyrosine, L-phenylalanyl-(2S)-2-phenylglycyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220808-23-1

CMF C30 H35 N3 O5

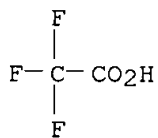
Absolute stereochemistry.



CM 2

CRN 76-05-1

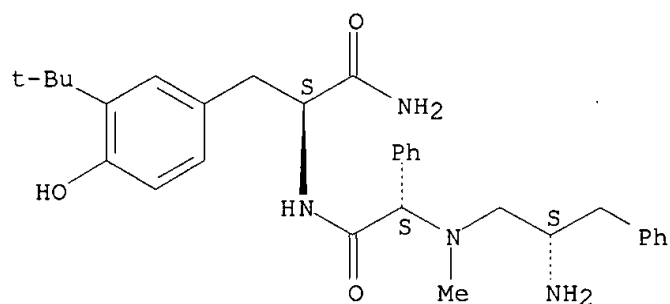
CMF C2 H F3 O2



RN 220808-25-3 CAPLUS

CN L-Tyrosinamide, (2S)-N-[(2S)-2-amino-3-phenylpropyl]-N-methyl-2-phenylglycyl-3-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT **220808-71-9P**

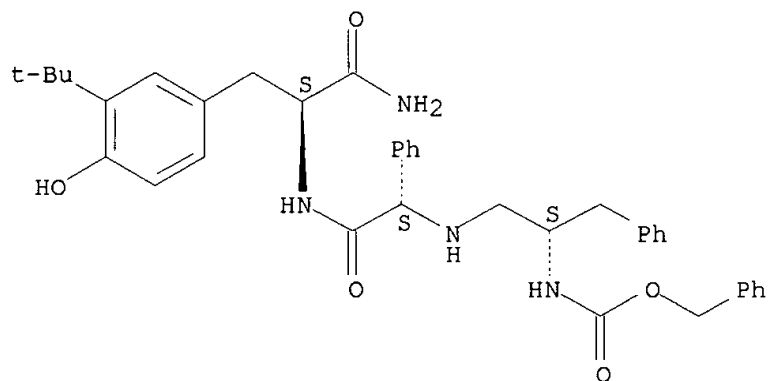
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of 3-tert-butyl-L-tyrosinamide-contg. peptide compds. as motilin receptor antagonists, inhibitors of digestive tract motility, and remedy for high blood motilin)

RN 220808-71-9 CAPLUS

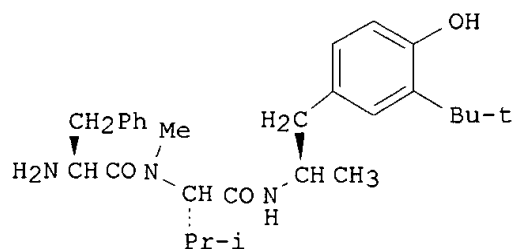
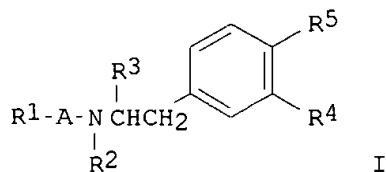
CN L-Tyrosinamide, (2S)-2-phenyl-N-[(2S)-3-phenyl-2-[[ (phenylmethoxy) carbonyl] amino]propyl]glycyl-3-(1,1-dimethylethyl)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



GI





AB Phenethylamine derivs. represented by general formula [I; wherein A represents an amino acid or .alpha.-substituted amino acid residue; R1 represents R6CO, (un)substituted C2-7 linear or branched alkyl, C3-8 alkenyl, or C3-8 alkynyl; R2 represents hydrogen, C1-3 linear or branched alkyl; R3 represents COR7, (un)substituted C1-5 linear or branched alkyl, C2-5 alkenyl, or C2-5 alkynyl; R4 represents H, C1-6 linear or branched alkyl, C2-6 alkenyl, C2-6 alkynyl, etc.; R5 represents hydroxy or C1-4 n-alkoxy; R6 represents (un)substituted C1-6 linear or branched alkyl, C2-7 alkenyl, or C2-7 alkynyl, optionally benzene- or heterocyclic ring-condensed C3-7 cycloalkyl, (un)substituted C6-12 arom. ring, (un)substituted C3-12 (un)satd. heterocyclic ring, (un)substituted NH2, (un)substituted linear or branched C1-5 alkoxy, C2-6 alkenyloxy, C2-6 alkynyloxy, etc.; and R7 represents H, (un)substituted C1-5 linear or branched alkyl, C3-7 cycloalkyl, (un)substituted NH2, OH, linear or branched alkyl C1-6 alkoxy, or C3-7 cycloalkyloxy] are prepd. Also claimed are a motilin receptor antagonist, an inhibitor of digestive tract motility, and a remedy for high blood motilin. They are also useful for the treatment of irritable bowel syndrome. Thus, N.alpha.-methyl-N-[2-(3-tert-butyl-4-hydroxyphenyl)-1-methylethyl]-L-valinamide was condensed with Boc-Phe-OH using HOBT and DIC in DMF at room temp. for 2.5 days followed by deprotection with CF3CO2H in CH2Cl2 to give the title compd. (II). II in vitro showed IC50 of 1.9 nM for inhibiting the binding of [125I]motilin motilin receptor prepn. from rabbit ileum mucus membrane.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 44 OF 148 CAPLUS COPYRIGHT 2003 ACS

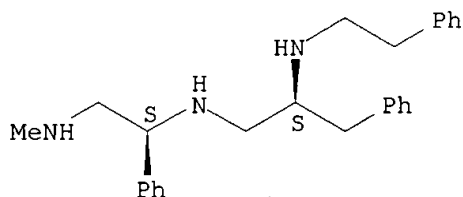
AN 1999:50263 CAPLUS

DN 130:196468

TI Parallel solid phase synthesis of tetrasubstituted diethylenetriamines via selective amide alkylation and exhaustive reduction of N-acylated dipeptides

AU Nefzi, Adel; Ostresh, John M.; Houghten, Richard A.  
CS Torrey Pines Institute for Molecular Studies, San Diego, CA, 92121, USA  
SO Tetrahedron (1999), 55(2), 335-344  
CODEN: TETRAB; ISSN: 0040-4020  
PB Elsevier Science Ltd.  
DT Journal  
LA English  
OS CASREACT 130:196468  
IT **220684-81-1P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(parallel solid phase synthesis of tetrasubstituted diethylenetriamines  
via selective amide alkylation and redn. of N-acylated dipeptides)  
RN 220684-81-1 CAPLUS  
CN 1,2-Propanediamine, N1-[(1S)-2-(methylamino)-1-phenylethyl]-3-phenyl-N2-(2-phenylethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

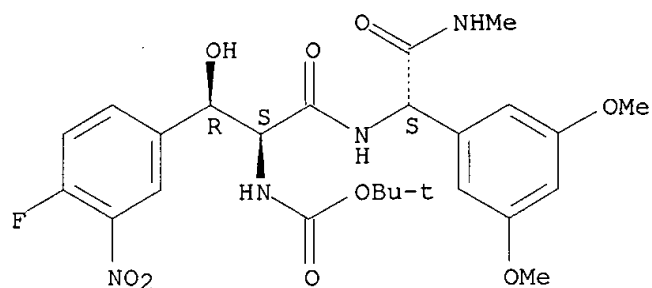


AB Polyamines are a rapidly developing area of vital importance to biomedical science. Selective N-alkylation followed by N-terminal acylation and the complete redn. of carbonyl amide bonds enables the prepn. by parallel solid phase synthesis of a wide range of N1,N5,1,4-tetrasubstituted-1,5-diamino-3-azapentane derivs.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 45 OF 148 CAPLUS COPYRIGHT 2003 ACS  
AN 1998:726885 CAPLUS  
DN 130:81859  
TI Total syntheses of vancomycin and eremomycin aglycons  
AU Evans, David A.; Wood, Michael R.; Trotter, B. Wesley; Richardson, Timothy I.; Barrow, James C.; Katz, Jeffrey L.  
CS Department of Chemistry & Chemical Biology, Harvard University, Cambridge, MA, 02138, USA  
SO Angewandte Chemie, International Edition (1998), 37(19), 2700-2704  
CODEN: ACIEF5; ISSN: 1433-7851  
PB Wiley-VCH Verlag GmbH  
DT Journal  
LA English  
IT **218901-86-1P 218901-87-2P 218901-88-3P**  
**218902-10-4P 218902-11-5P 218902-12-6P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(total syntheses of vancomycin and eremomycin aglycons)  
RN 218901-86-1 CAPLUS  
CN Glycinamide, (.beta.R)-N-[(1,1-dimethylethoxy)carbonyl]-4-fluoro-.beta.-hydroxy-3-nitro-L-phenylalanyl-2-(3,5-dimethoxyphenyl)-N-methyl-, (2S)- (9CI) (CA INDEX NAME)

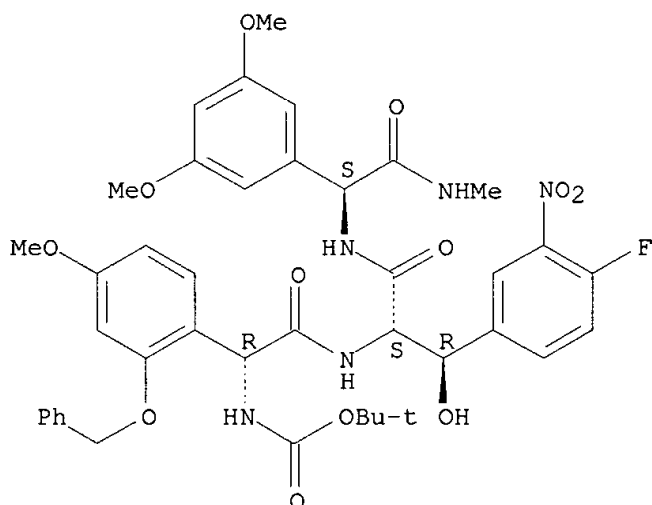
Absolute stereochemistry. Rotation (+).



RN 218901-87-2 CAPLUS

CN Glycinamide, (2R)-N-[(1,1-dimethylethoxy)carbonyl]-2-[4-methoxy-2-(phenylmethoxy)phenyl]glycyl-(.beta.R)-4-fluoro-.beta.-hydroxy-3-nitro-L-phenylalanyl-2-(3,5-dimethoxyphenyl)-N-methyl-, (2S)- (9CI) (CA INDEX NAME)

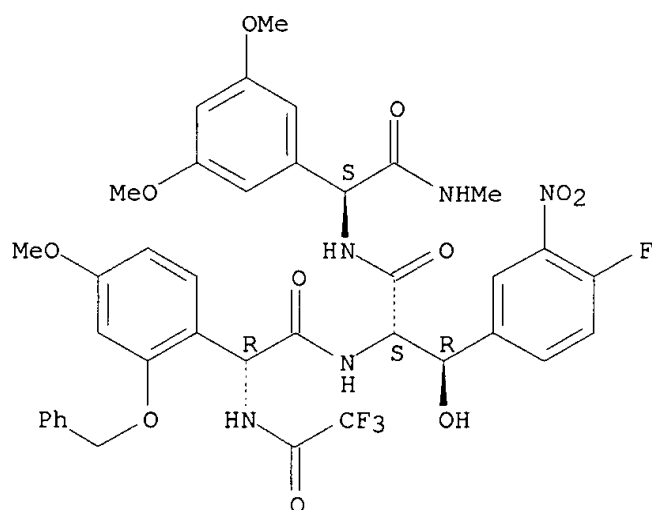
Absolute stereochemistry. Rotation (-).



RN 218901-88-3 CAPLUS

CN Glycinamide, (2R)-2-[4-methoxy-2-(phenylmethoxy)phenyl]-N-(trifluoroacetyl)glycyl-(.beta.R)-4-fluoro-.beta.-hydroxy-3-nitro-L-phenylalanyl-2-(3,5-dimethoxyphenyl)-N-methyl-, (2S)- (9CI) (CA INDEX NAME)

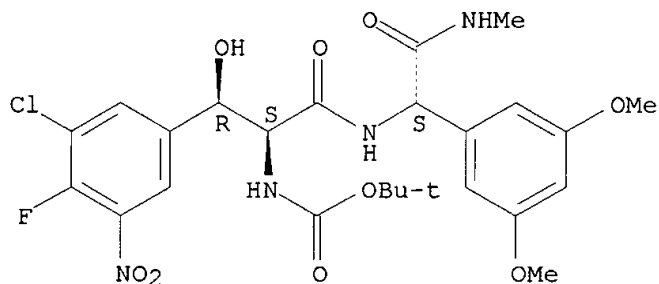
Absolute stereochemistry. Rotation (+).



RN 218902-10-4 CAPLUS

CN Glycinamide, (.beta.R)-3-chloro-N-[(1,1-dimethylethoxy)carbonyl]-4-fluoro-.beta.-hydroxy-5-nitro-L-phenylalanyl-2-(3,5-dimethoxyphenyl)-N-methyl-, (2S)- (9CI) (CA INDEX NAME)

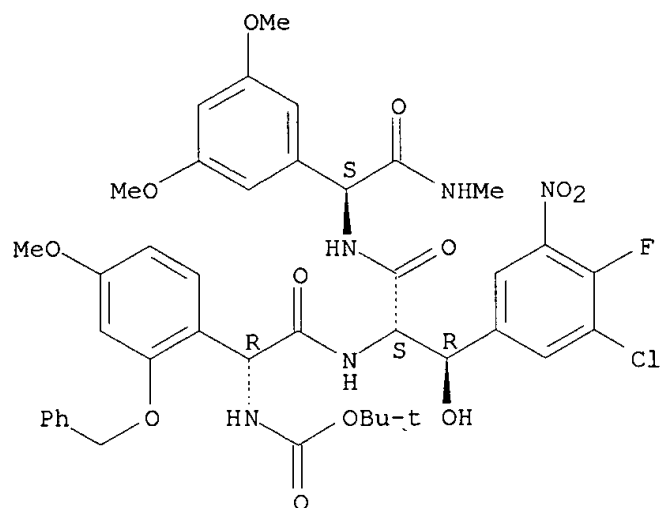
Absolute stereochemistry. Rotation (+).



RN 218902-11-5 CAPLUS

CN Glycinamide, (2R)-N-[(1,1-dimethylethoxy)carbonyl]-2-[4-methoxy-2-(phenylmethoxy)phenyl]glycyl-(.beta.R)-3-chloro-4-fluoro-.beta.-hydroxy-5-nitro-L-phenylalanyl-2-(3,5-dimethoxyphenyl)-N-methyl-, (2S)- (9CI) (CA INDEX NAME)

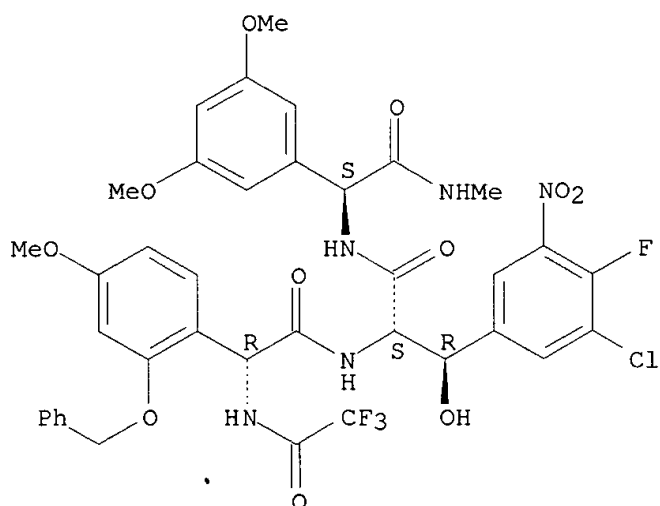
Absolute stereochemistry. Rotation (-).



RN 218902-12-6 CAPLUS

CN Glycinamide, (2R)-2-[4-methoxy-2-(phenylmethoxy)phenyl]-N-(trifluoroacetyl)glycyl-(.beta.R)-3-chloro-4-fluoro-.beta.-hydroxy-5-nitro-L-phenylalanyl-2-(3,5-dimethoxyphenyl)-N-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



AB The first syntheses of the vancomycin aglycon and the eremomycin aglycon are reported. Relevant methodol. includes new asym. amino acid syntheses and new macrocyclization reactions amenable to the construction of macrocyclic diaryl ether and biaryl-contg. tripeptides. The detailed route given provides vancomycin aglycon in 40 steps (longest linear sequence) from 3,5-dimethoxybenzyl alc. These syntheses provide diastereoselective solns. to each of the biaryl ether and biaryl macrocycles and define a convergent assemblage process which can be extended to a variety of natural and unnatural analogs in the vancomycin

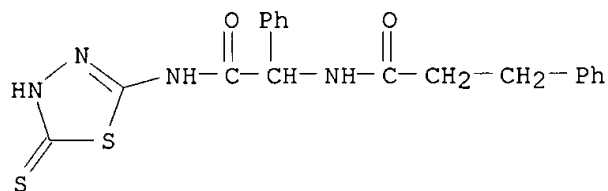
series.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

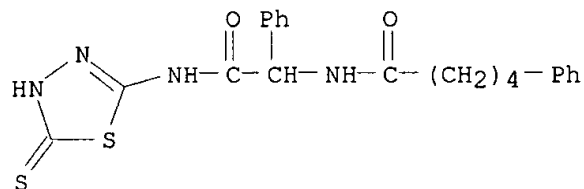
L4 ANSWER 46 OF 148 CAPLUS COPYRIGHT 2003 ACS  
AN 1998:719133 CAPLUS  
DN 129:331046  
TI Preparation of amino acid thiadiazole amide MMP inhibitors  
IN Mitchell, Mark Allen; Schostarez, Heinrich Josef; Maggiora, Linda Louise;  
Lindberg, Thomas J.  
PA USA  
SO U.S., 27 pp.  
CODEN: USXXAM  
DT Patent  
LA English  
FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
|    | -----      | ---  | -----    | -----           | -----    |
| PI | US 5830869 | A    | 19981103 | US 1997-878266  | 19970618 |
|    |            |      |          | US 1997-878266  | 19970618 |

OS MARPAT 129:331046  
IT **200642-32-6P 200642-33-7P**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of amino acid thiadiazole amide MMP inhibitors)  
RN 200642-32-6 CAPLUS  
CN Benzenepropanamide, N-[2-[(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)amino]-2-oxo-1-phenylethyl]- (9CI) (CA INDEX NAME)



RN 200642-33-7 CAPLUS  
CN Benzenepentanamide, N-[2-[(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)amino]-2-oxo-1-phenylethyl]- (9CI) (CA INDEX NAME)



AB Amino acid derivs. R2CONH-Q-CONHR1 [R1 = 4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl; Q = (un)substituted methylene, ethylene, 1,2-cyclopropanediyl, -cyclobutanediyl, -cyclopentanedyl, or

-cyclohexanediyl; R2 = alkyl, (un)substituted Ph or phenylalkyl, 3-indolylalkyl, 9H-fluoren-9-ylmethoxy, alkoxyalkyl, 1-tert-butoxycarbonyl-2-pyrrolyl] were prepd. as MMP inhibitors. Thus, Cbz-NHCHPhCONHR1 (Cbz = benzyloxycarbonyl, same R1), prepd. by amidation reaction, showed  $K_i = 1.21 \mu\text{M}$  for inhibition of stromelysin.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 47 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1998:625620 CAPLUS

DN 129:316000

TI Synthesis of enantiopure homoallylic alcohols by a highly selective asymmetric allylation of ketones

AU Tietze, Lutz F.; Schiemann, Kai; Wegner, Christoph; Wulff, Christian

CS Institute Organic Chemistry, Georg-August-Universitat Gottingen, Gottingen, D-37077, Germany

SO Chemistry--A European Journal (1998), 4(9), 1862-1869

CODEN: CEUJED; ISSN: 0947-6539

PB Wiley-VCH Verlag GmbH

DT Journal

LA English

OS CASREACT 129:316000

IT 165823-95-0P

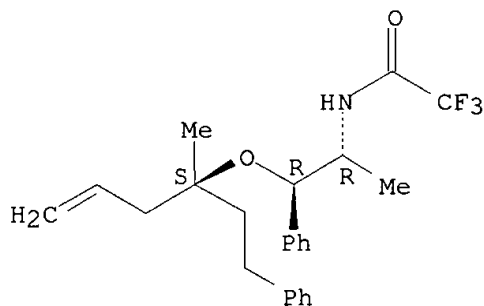
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of enantiopure homoallylic alcs. by asym. allylation of ketones)

RN 165823-95-0 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[[(1S)-1-methyl-1-(2-phenylethyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB A highly selective asym. domino allylation of aliph. ketones is described. When Me ketones, (R,R)-Me<sub>2</sub>SiOCHPhCHMeNHCOCF<sub>3</sub>, and CH<sub>2</sub>:CHCH<sub>2</sub>SiMe<sub>3</sub> react in the presence of catalytic amts. of trifluoromethanesulfonic acid, the homoallylic ethers are produced with up to 24:1 diastereoselectivity and 89% yield. Ether cleavage using lithium or sodium in liq. ammonia gives the homoallylic alcs. in 75 to 95% yield and up to 92% ee. Even EtCOMe, the most difficult example, showed a stereoselectivity of 9:1 at -78.degree.C and 24:1 at -109.degree.C. In addn., the allylation of protected hydroxyalkyl Me ketones gave the corresponding homoallylic ethers with a diastereoselectivity of up to >244:1 and 98% yield. In contrast, Et alkyl ketones have a low selectivity.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 48 OF 148 CAPLUS COPYRIGHT 2003 ACS  
AN 1998:479505 CAPLUS  
DN 129:122870  
TI Preparation of cycloalkyl, lactam, lactone and related compounds for  
inhibiting .beta.-amyloid peptide release and/or its synthesis  
IN Wu, Jing; Tung, Jay S.; Thorsett, Eugene D.; Pleiss, Michael A.; Nissen,  
Jeffrey S.; Neitz, Jeffrey; Latimer, Lee H.; John, Varghese; Freedman,  
Stephen; Britton, Thomas C.; Audia, James E.; Reel, Jon K.; Mabry, Thomas  
E.; Dressman, Bruce A.; Cwi, Cynthia L.; Droste, James J.; Henry, Steven  
S.; Mcdaniel, Stacey L.; Scott, William Leonard; Stucky, Russell D.;  
Porter, Warren J.  
PA Athena Neurosciences, Inc., USA; Eli Lilly & Co.  
SO PCT Int. Appl., 889 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 2

|    | PATENT NO.    | KIND   | DATE     | APPLICATION NO.  | DATE        |
|----|---------------|--|----------|------------------|-------------|
| PI | WO 9828268    | A2   | 19980702 | WO 1997-US22986  | 19971222    |
|    | WO 9828268    | A3   | 19981008 |                  |             |
|    | W:            | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                  |             |
|    | RW:           | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG   |          |                  |             |
|    |               |  |          | US 1996-64851P   | P 19961223  |
|    |               |  |          | US 1996-64851P   | P 19961223  |
|    |               |  |          | US 1996-780025   | A1 19961223 |
|    | ZA 9711537    | A  | 19980625 | ZA 1997-11537    | 19971222    |
|    |               |  |          | US 1996-780025   | A 19961223  |
|    | AU 9857007    | A1   | 19980717 | AU 1998-57007    | 19971222    |
|    | AU 749658     | B2   | 20020627 |                  |             |
|    |               |  |          | US 1996-780025   | A 19961223  |
|    |               |  |          | WO 1997-US22986W | 19971222    |
|    | EP 951466     | A2   | 19991027 | EP 1997-953208   | 19971222    |
|    | R:            | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |          |                  |             |
|    |               |  |          | US 1996-780025   | A 19961223  |
|    |               |  |          | WO 1997-US22986W | 19971222    |
|    | CN 1242007    | A  | 20000119 | CN 1997-180901   | 19971222    |
|    |               |  |          | US 1996-780025   | A 19961223  |
|    | BR 9714517    | A  | 20000704 | BR 1997-14517    | 19971222    |
|    |               |  |          | US 1996-780025   | A 19961223  |
|    |               |  |          | WO 1997-US22986W | 19971222    |
|    | JP 2000511932 | T2   | 20000912 | JP 1998-528867   | 19971222    |
|    |               |  |          | US 1996-780025   | A 19961223  |
|    |               |  |          | WO 1997-US22986W | 19971222    |
|    | NZ 335583     | A  | 20010330 | NZ 1997-335583   | 19971222    |
|    |               |  |          | US 1996-780025   | A 19961223  |
|    |               |  |          | WO 1997-US22986W | 19971222    |



|               |    |          |                   |          |
|---------------|----|----------|-------------------|----------|
| MX 9905844    | A  | 20000731 | MX 1999-5844      | 19990621 |
|               |    |          | US 1996-780025 A  | 19961223 |
|               |    |          | WO 1997-US22986W  | 19971222 |
| NO 9903098    | A  | 19990820 | NO 1999-3098      | 19990622 |
|               |    |          | US 1996-780025 A  | 19961223 |
|               |    |          | WO 1997-US22986W  | 19971222 |
| US 2002045747 | A1 | 20020418 | US 2001-916282    | 20010730 |
|               |    |          | US 1996-64851P P  | 19961223 |
|               |    |          | US 1996-780025 A  | 19961223 |
|               |    |          | US 1997-996422 A3 | 19971222 |
| US 2002055500 | A1 | 20020509 | US 2001-916440    | 20010730 |
|               |    |          | US 1996-64851P P  | 19961223 |
|               |    |          | US 1996-780025 A  | 19961223 |
|               |    |          | US 1997-996422 A3 | 19971222 |

## PATENT FAMILY INFORMATION:

FAN 1999:425778

|               | PATENT NO. | KIND   | DATE              | APPLICATION NO.  | DATE     |
|---------------|------------|--|-------------------|------------------|----------|
| PI            | WO 9932453 | A1   | 19990701          | WO 1998-US22637  | 19981029 |
|               | W:         | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |                   |                  |          |
|               | RW:        | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |                   |                  |          |
|               |            |  |                   | US 1996-64851P P | 19961223 |
|               |            |  |                   | US 1997-996422 A | 19971222 |
|               |            |  |                   | US 1998-102726 A | 19980622 |
| CA 2307221    | AA         | 19990701   | CA 1998-2307221   | 19981029         |          |
|               |            |  | US 1997-996422 A  | 19971222         |          |
|               |            |  | US 1998-102726 A  | 19980622         |          |
|               |            |  | WO 1998-US22637W  | 19981029         |          |
| AU 9912777    | A1         | 19990712   | AU 1999-12777     | 19981029         |          |
|               |            |  | US 1997-996422 A  | 19971222         |          |
|               |            |  | US 1998-102726 A  | 19980622         |          |
|               |            |  | WO 1998-US22637W  | 19981029         |          |
| BR 9812773    | A          | 20001010   | BR 1998-12773     | 19981029         |          |
|               |            |  | US 1997-996422 A  | 19971222         |          |
|               |            |  | US 1998-102726 A  | 19980622         |          |
|               |            |  | WO 1998-US22637W  | 19981029         |          |
| EP 1042298    | A1         | 20001011   | EP 1998-956198    | 19981029         |          |
|               | R:         | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |                   |                  |          |
|               |            |  | US 1997-996422 A  | 19971222         |          |
|               |            |  | US 1998-102726 A  | 19980622         |          |
|               |            |  | WO 1998-US22637W  | 19981029         |          |
| US 2002068741 | A1         | 20020606   | US 2001-915263    | 20010726         |          |
|               |            |  | US 1996-64851P P  | 19961223         |          |
|               |            |  | US 1997-996422 A3 | 19971222         |          |
| US 2002052359 | A1         | 20020502   | US 2001-915480    | 20010727         |          |
| US 6544978    | B2         | 20030408   |                   |                  |          |
|               |            |  | US 1996-64851P P  | 19961223         |          |
|               |            |  | US 1997-996422 A3 | 19971222         |          |
| US 2002111343 | A1         | 20020815   | US 2001-915547    | 20010727         |          |

|               |    |          |                           |
|---------------|----|----------|---------------------------|
| US 2002115652 | A1 | 20020822 | US 1996-64851P P 19961223 |
| US 6541466    | B2 | 20030401 | US 1997-996422 A319971222 |
|               |    |          | US 2001-915362 20010727   |
| US 2002123486 | A1 | 20020905 | US 1996-64851P P 19961223 |
|               |    |          | US 1997-996422 A319971222 |
|               |    |          | US 2001-915342 20010727   |
| US 2002137738 | A1 | 20020926 | US 1996-64851P P 19961223 |
| US 6559141    | B2 | 20030506 | US 1997-996422 A319971222 |
|               |    |          | US 2001-915564 20010727   |
| US 2002151538 | A1 | 20021017 | US 1996-64851P P 19961223 |
|               |    |          | US 1997-996422 A319971222 |
|               |    |          | US 2001-915379 20010727   |
| US 2002173504 | A1 | 20021121 | US 1996-64851P P 19961223 |
|               |    |          | US 1997-996422 A319971222 |
|               |    |          | US 2001-915519 20010727   |
| US 2002045747 | A1 | 20020418 | US 1996-64851P P 19961223 |
|               |    |          | US 1997-996422 A319971222 |
|               |    |          | US 2001-916282 20010730   |
| US 2002055500 | A1 | 20020509 | US 1996-64851P P 19961223 |
|               |    |          | US 1996-780025 A 19961223 |
|               |    |          | US 1997-996422 A319971222 |
|               |    |          | US 2001-916440 20010730   |
|               |    |          | US 1996-64851P P 19961223 |
|               |    |          | US 1996-780025 A 19961223 |
|               |    |          | US 1997-996422 A319971222 |

OS MARPAT 129:122870

IT **209988-54-5P 209988-58-9P**

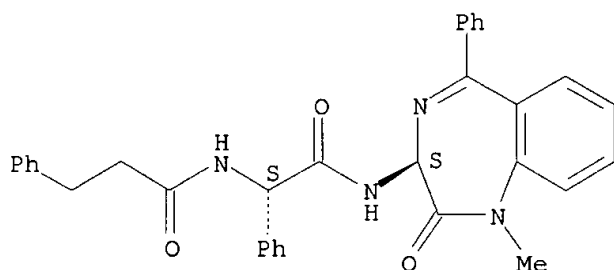
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of cycloalkyl, lactam, lactone and related compds. for inhibiting .beta.-amyloid peptide release and/or its synthesis)

RN 209988-54-5 CAPLUS

CN Benzenepropanamide, N-[(1S)-2-[[[(3S)-2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]amino]-2-oxo-1-phenylethyl]- (9CI) (CA INDEX NAME)

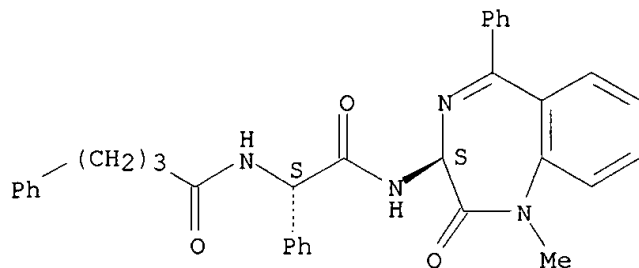
Absolute stereochemistry.



RN 209988-58-9 CAPLUS

CN Benzenebutanamide, N-[(1S)-2-[[[(3S)-2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]amino]-2-oxo-1-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Disclosed are compds.  $R_1ZmNHYNCHpR_2C(X)R_3$  [ $R_1$  = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, or cycloalkenyl or aryl, heteroaryl, or heterocyclic;  $R_2$  and  $R_3$  form a cycloalkyl, cycloalkenyl, heterocyclic, substituted cycloalkyl, or substituted cycloalkenyl ring which is optionally fused;  $X$  = oxo, thioxo, hydroxyl, thiol, or hydro;  $Y$  =  $CHR_4CONH$  where  $R_4$  = (un)substituted alkyl, alkenyl, or alkynyl or cycloalkyl, aryl, heteroaryl, or heterocyclic;  $Z$  is  $TCX'X''CO$  where  $T$  is a bond, O, S,  $NR_5$  ( $R_5$  = H, acyl, alkyl, aryl, or heteroaryl),  $X'$  and  $X''$  are H, OH, or F or  $X'X''$  = oxo;  $m, p = 0, 1$ ;  $n = 0, 1, 2$ ] which inhibit .beta.-amyloid peptide release and/or its synthesis, and, accordingly, have utility in treating Alzheimer's disease. Thus, 3-[[N'-(3,4-methylenedioxyphenylacetyl)-L-alaninyl]amino]-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one was prepd. by coupling of 3-(L-alaninylamino)-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one with 3,4-methylenedioxyphenylacetic acid.

L4 ANSWER 49 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1998:450863 CAPLUS

DN 129:149240

TI Synthesis of tripeptides containing .alpha.,.alpha.-diphenylglycine by the modified Ugi reaction

AU Yamada, Takashi; Omote, Yuichiro; Yamanaka, Yoshinori; Miyazawa, Toshifumi; Kuwata, Shigeru

CS Department Chemistry, Faculty Science, Konan University, Kobe, 658, Japan

SO Synthesis (1998), (7), 991-998

CODEN: SYNTBF; ISSN: 0039-7881

PB Georg Thieme Verlag

DT Journal

LA English

IT **142618-58-4P**

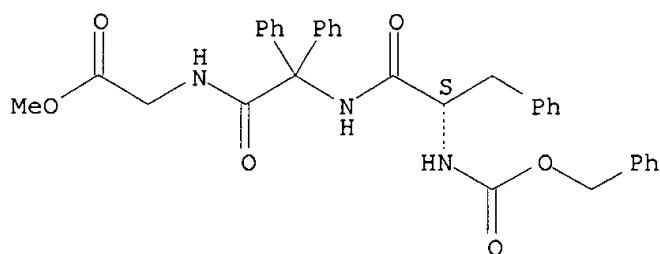
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of tripeptides contg. .alpha.,.alpha.-diphenylglycine by modified Ugi reaction)

RN 142618-58-4 CAPLUS

CN Glycine, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-2,2-diphenylglycyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB A modified Ugi reaction was developed to synthesize tripeptides contg. H<sub>2</sub>NCPH<sub>2</sub>CO<sub>2</sub>H (Dph) together with bulky amino acids. By the use of Ph<sub>2</sub>CNH, N-benzoxycarbonyl (Z) amino acids, and isocyanoacetates, crowded tripeptides such as Z-Aib-Dph-Aib-OMe, Z-Ac6c-Dph-Aib-OMe, and Z-(Dph)<sub>3</sub>-OMe, were synthesized.

L4 ANSWER 50 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1998:405971 CAPLUS

DN 129:81965

TI Preparation of peptidyl 5-amino-1,3,4-thiadiazole-2-thiones

IN Oleksyszyn, Jozef; Jacobson, Alan R.

PA Proscript, Inc., USA; Oleksyszyn, Jozef; Jacobson, Alan R.

SO PCT Int. Appl., 97 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | WO 9825949  | A1   | 19980618 | WO 1997-US22534 | 19971209 |
|    | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG |      |          |                 |          |
|    | AU 9856923  | A1   | 19980703 | US 1996-762503  | 19961209 |
|    |   |      |          | AU 1998-56923   | 19971209 |
|    |   |      |          | US 1996-762503  | 19961209 |
|    |   |      |          | WO 1997-US22534 | 19971209 |

OS MARPAT 129:81965

IT **186098-00-0P 186098-04-4P 186098-07-7P**

**186098-66-8P 186098-67-9P 209274-75-9P**

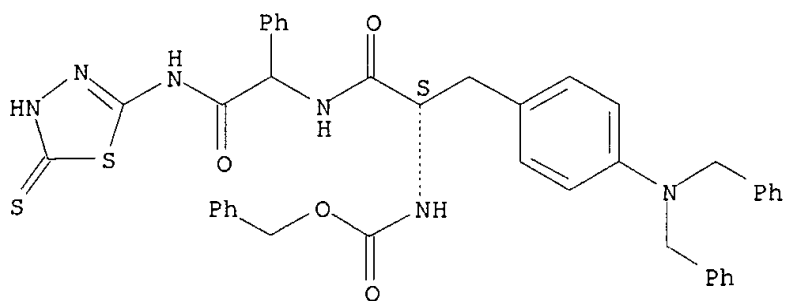
**209274-89-5P 209274-90-8P 209275-20-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of peptidyl aminothiadiazolethiones)

RN 186098-00-0 CAPLUS

CN Glycinamide, 4-[bis(phenylmethyl)amino]-N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl- (9CI) (CA INDEX NAME)

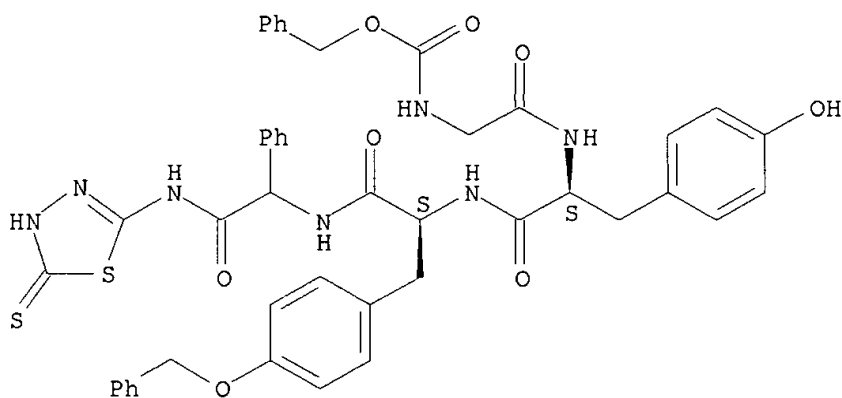
Absolute stereochemistry.



RN 186098-04-4 CAPLUS

CN Glycinamide, N-[(phenylmethoxy) carbonyl]glycyl-L-tyrosyl-O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl- (9CI)  
(CA INDEX NAME)

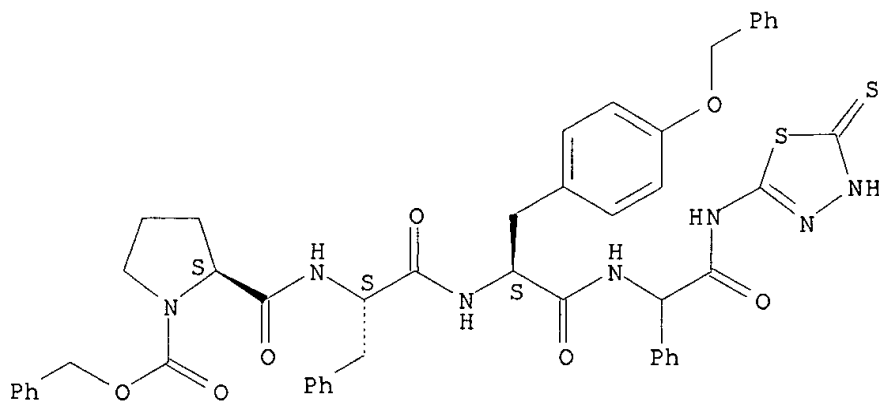
Absolute stereochemistry.

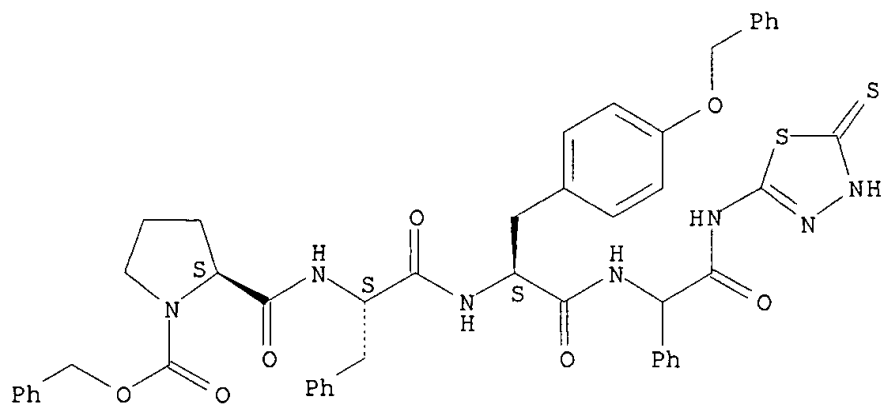


RN 186098-07-7 CAPLUS

CN Glycinamide, 1-[(phenylmethoxy) carbonyl]-L-prolyl-L-phenylalanyl-O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

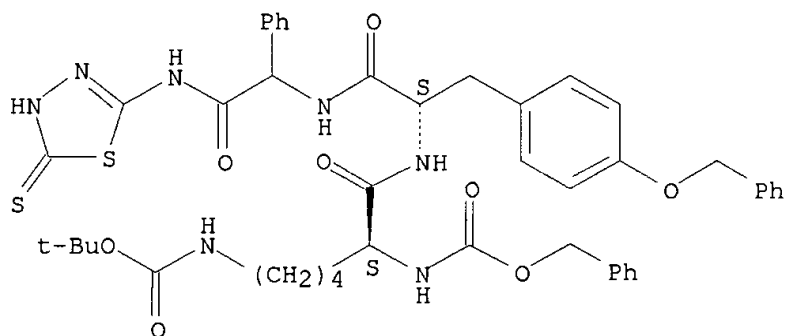




RN 186098-66-8 CAPLUS

CN Glycinamide, N6-[(1,1-dimethylethoxy)carbonyl]-N2-[(phenylmethoxy)carbonyl]-L-lysyl-O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl- (9CI) (CA INDEX NAME)

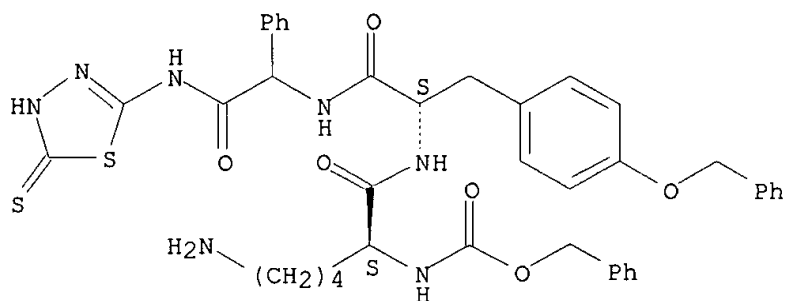
Absolute stereochemistry.



RN 186098-67-9 CAPLUS

CN Glycinamide, N2-[(phenylmethoxy)carbonyl]-L-lysyl-O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl- (9CI) (CA INDEX NAME)

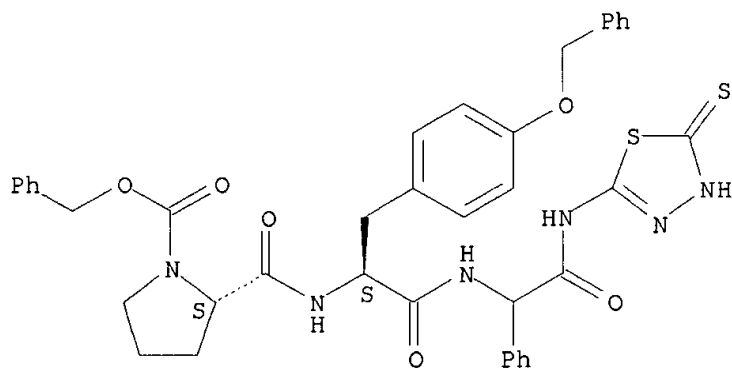
Absolute stereochemistry.



RN 209274-75-9 CAPLUS

CN Glycinamide, 1-[(phenylmethoxy)carbonyl]-L-prolyl-O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl- (9CI)  
(CA INDEX NAME)

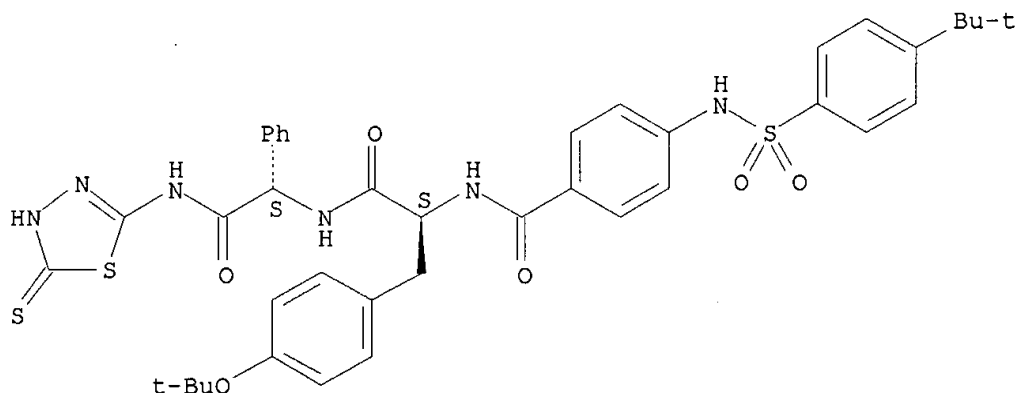
Absolute stereochemistry.



RN 209274-89-5 CAPLUS

CN Glycinamide, O-(1,1-dimethylethyl)-N-[4-[[[4-(1,1-dimethylethyl)phenyl]sulfonyl]amino]benzoyl]-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

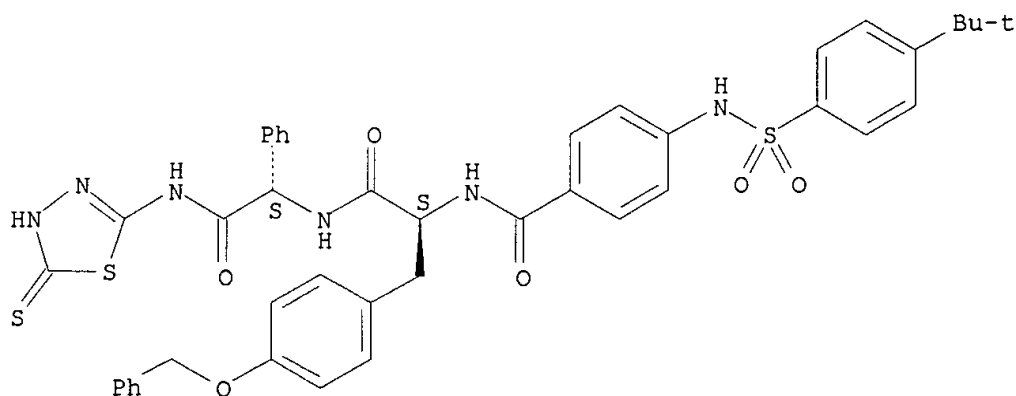
Absolute stereochemistry.



RN 209274-90-8 CAPLUS

CN Glycinamide, N-[4-[[[4-(1,1-dimethylethyl)phenyl]sulfonyl]amino]benzoyl]-O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

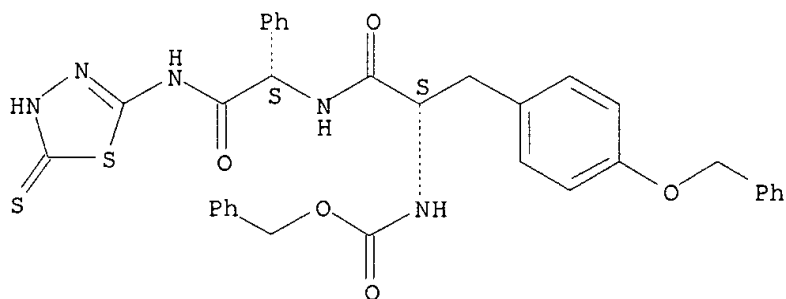
Absolute stereochemistry.



RN 209275-20-7 CAPLUS

CN Glycinamide, N-[(phenylmethoxy)carbonyl]-O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



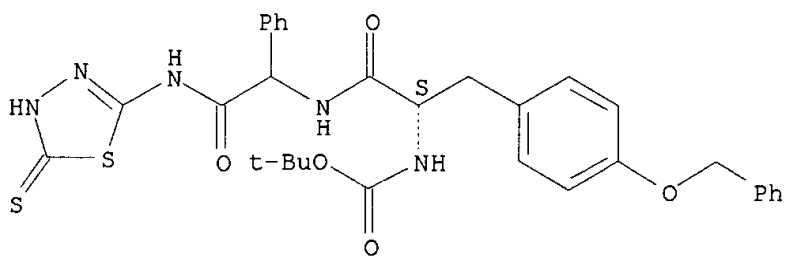
IT 186098-36-2P 186098-37-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of peptidyl aminothiadiazoethiones)

RN 186098-36-2 CAPLUS

CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl-, (9CI) (CA INDEX NAME)

Absolute stereochemistry.

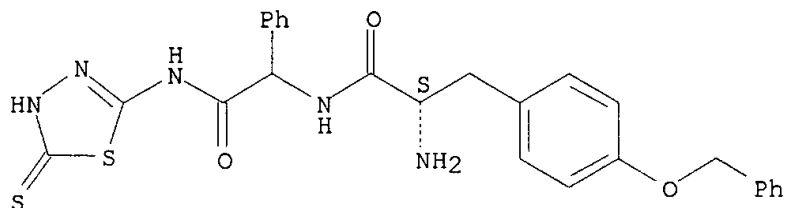




RN 186098-37-3 CAPLUS

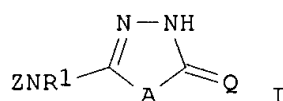
CN Glycinamide, O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

GI



AB Aminothiadiazoethiones I (Q, A = S, O and one of Q and A is S; R1 = H, alkyl, acyl; Z is an org. radical that does not substantially interfere with matrix metalloproteinase inhibitory activity) were prepd. Thus, 5-[N-[4-(4-tert-butylphenylsulfonylamino)benzoyl]phenylalanylvalylamino]-1,3,4-thiadiazole-2-thione, prepd. by acylation of 5-amino-1,3,4-thiadiazole-2-thione with the phenylalanylvaline deriv., was assayed for stromelysin inhibitory activity (IC50 = 44 nM).

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 51 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1998:352865 CAPLUS

DN 129:54603

TI Preparation of antiviral peptide derivatives

IN Attwood, Michael Richard; Hurst, David Nigel; Jones, Philip Stephen; Kay, Paul Brittain; Raynham, Tony Michael; Wilson, Francis Xavier

PA F. Hoffmann-La Roche A.-G., Switz.

SO PCT Int. Appl., 132 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|------------|------|----------|-----------------|----------|
| WO 9822496 | A2   | 19980528 | WO 1997-EP6189  | 19971107 |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,  
 UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,  
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 GN, ML, MR, NE, SN, TD, TG

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|-----------------------|----|----------|----------------|----|----------|
| AU 9855510            | A1 | 19980610 | GB 1996-23908  | A  | 19961118 |
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| EP 941233             | A2 | 19990915 | WO 1997-EP6189 | W  | 19971107 |
| R: DE, ES, FR, GB, IT |    |          | EP 1997-951869 |    | 19971107 |
|                       |    |          | GB 1996-23908  | A  | 19961118 |
|                       |    |          | WO 1997-EP6189 | W  | 19971107 |
| JP 2000508344         | T2 | 20000704 | JP 1998-523153 |    | 19971107 |
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| ZA 9710156            | A  | 19980518 | ZA 1997-10156  |    | 19971111 |
|                       |    |          | GB 1996-23908  | A  | 19961118 |
| US 5866684            | A  | 19990202 | US 1997-971036 |    | 19971114 |
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| US 6018020            | A  | 20000125 | US 1998-96570  |    | 19980612 |
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OS MARPAT 129:54603

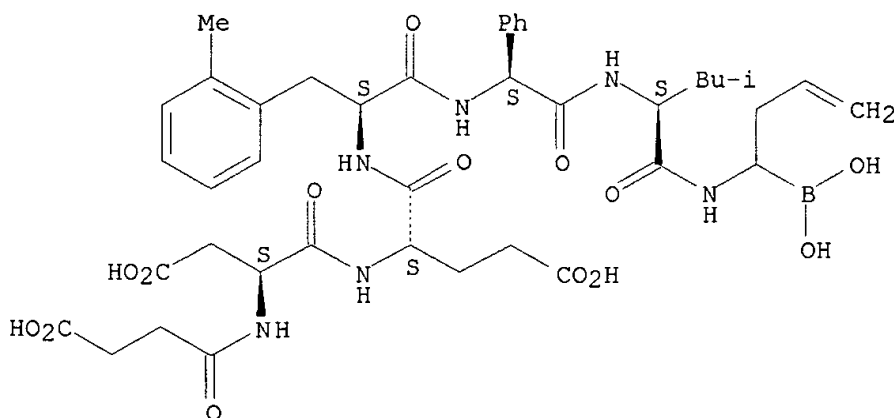
IT **208520-30-3P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of antiviral peptide derivs.)

RN 208520-30-3 CAPLUS

CN L-Leucinamide, N-(3-carboxy-1-oxopropyl)-L-.alpha.-aspartyl-L-.alpha.-glutamyl-2-methyl-L-phenylalanyl-(2S)-2-phenylglycyl-N-(1-borono-3-butenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **208521-66-8P 208521-67-9P 208521-68-0P**

**208521-69-1P 208521-70-4P 208521-84-0P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

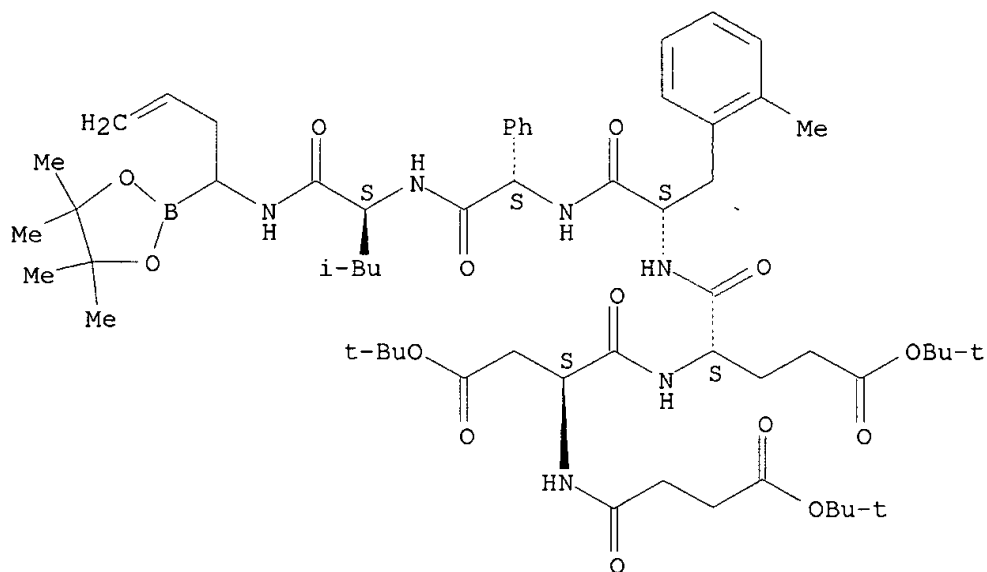
(Reactant or reagent)

(prepn. of antiviral peptide derivs.)

RN 208521-66-8 CAPLUS

CN L-Leucinamide, N-[4-(1,1-dimethylethoxy)-1,4-dioxobutyl]-L-.alpha.-  
aspartyl-L-.alpha.-glutamyl-2-methyl-L-phenylalanyl-(2S)-2-phenylglycyl-N-  
[1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-butenyl]-,  
bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

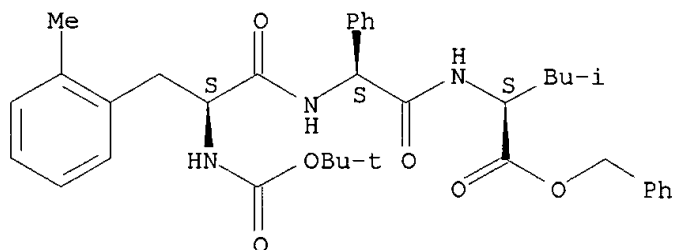
Absolute stereochemistry.



RN 208521-67-9 CAPLUS

CN L-Leucine, N-[(1,1-dimethylethoxy)carbonyl]-2-methyl-L-phenylalanyl-(2S)-2-  
phenylglycyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

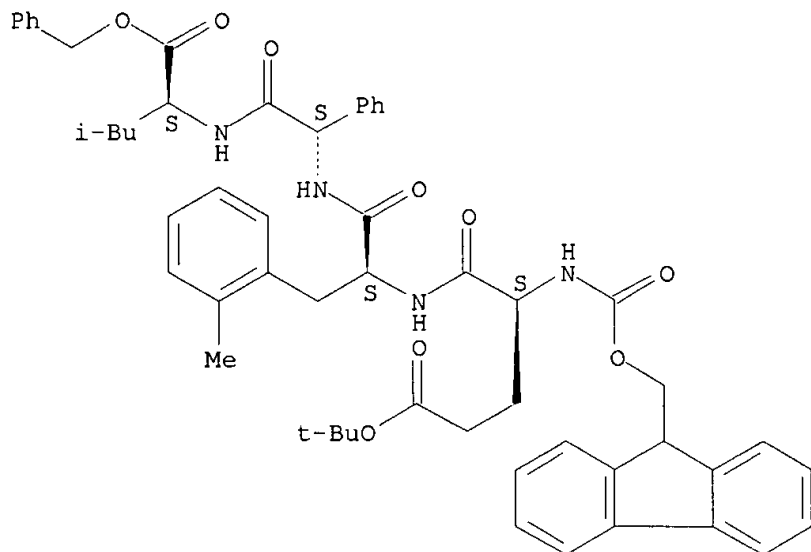
Absolute stereochemistry.



RN 208521-68-0 CAPLUS

CN L-Leucine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-.alpha.-glutamyl-2-  
methyl-L-phenylalanyl-(2S)-2-phenylglycyl-, 1-(1,1-dimethylethyl)  
4-(phenylmethyl) ester (9CI) (CA INDEX NAME)

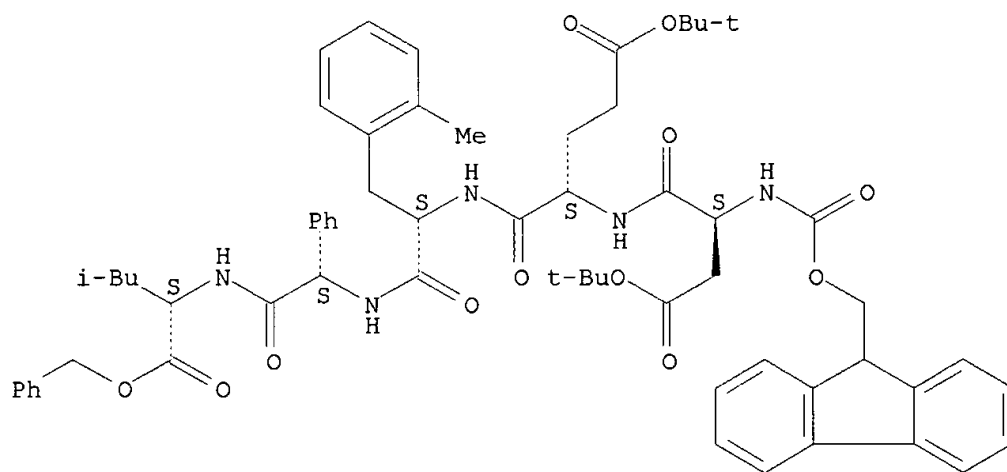
Absolute stereochemistry.



RN 208521-69-1 CAPLUS

CN L-Leucine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-.alpha.-aspartyl-L-.alpha.-glutamyl-2-methyl-L-phenylalanyl-(2S)-2-phenylglycyl-, 1,2-bis(1,1-dimethylethyl) 5-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

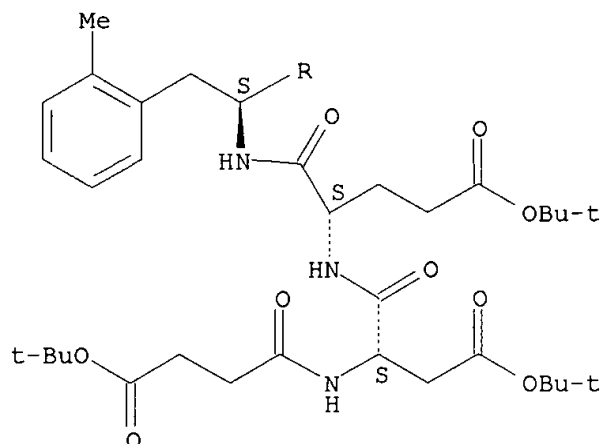


RN 208521-70-4 CAPLUS

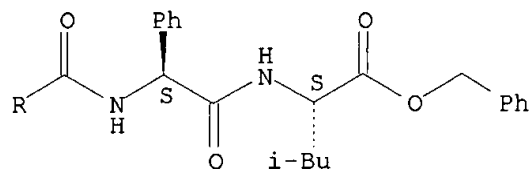
CN L-Leucine, N-[4-(1,1-dimethylethoxy)-1,4-dioxobutyl]-L-.alpha.-aspartyl-L-.alpha.-glutamyl-2-methyl-L-phenylalanyl-(2S)-2-phenylglycyl-, 1,2-bis(1,1-dimethylethyl) 5-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



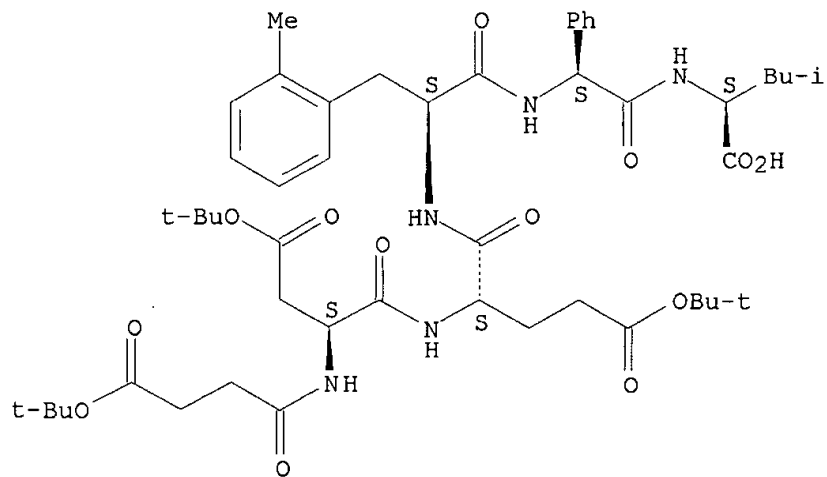
PAGE 2-A



RN 208521-84-0 CAPLUS

CN L-Leucine, N-[4-(1,1-dimethylethoxy)-1,4-dioxobutyl]-L-.alpha.-aspartyl-L-.alpha.-glutamyl-2-methyl-L-phenylalanyl-(2S)-2-phenylglycyl-, 1,2-bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Peptides R<sub>9</sub>NHCHR<sub>8</sub>CONHCHR<sub>7</sub>CONR<sub>6</sub>CHR<sub>5</sub>CONHCHR<sub>4</sub>CONR<sub>3</sub>CHR<sub>2</sub>CONHCHRR<sub>1</sub> [R = CHO or B(OH)<sub>2</sub>; R<sub>1</sub> = optionally substituted alkyl, alkenyl, alkynyl; R<sub>2</sub> = optionally substituted alkyl; R<sub>3</sub> = H, alkyl; or R<sub>2</sub> and R<sub>3</sub> together represent di- or trimethylene optionally substituted by hydroxy; R<sub>4</sub> = optionally substituted alkyl, alkenyl, aryl, cycloalkyl; R<sub>5</sub> = optionally substituted alkyl, cycloalkyl; R<sub>6</sub> = H, alkyl; R<sub>7</sub> = optionally substituted alkyl, cycloalkyl; R<sub>8</sub> = optionally substituted alkyl; R<sub>9</sub> = alkylcarbonyl, carboxyalkylcarbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, alkoxy carbonyl, arylalkoxy carbonyl] or their salts were prepd. for use as antiviral agents. Thus, 2(RS)-[N-[N-[N-[N-[N-(3-carboxypropionyl)-L-.alpha.-aspartyl]-L-.alpha.-glutamyl]-2-methyl-L-phenylalanyl]-3-methyl-L-valyl]-L-leucyl]amino]-4-pentenaldehyde, prepd. via intermediate N-[N-[N-[N-[N-(3-tert-butoxycarbonyl)propionyl]-O-tert-butyl-L-.alpha.-aspartyl]-O-tert-butyl-L-.alpha.-glutamyl]-2-methyl-L-phenylalanyl]-3-methyl-L-valyl]-L-leucine, was assayed for inhibition of ACV protease (IC<sub>50</sub> = 0.09 .mu.Mol/l).

L4 ANSWER 52 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1998:215089 CAPLUS

DN 128:265810

TI Inhibition of Membrane-Type 1 Matrix Metalloproteinase by Hydroxamate Inhibitors: An Examination of the Subsite Pocket

AU Yamamoto, Minoru; Tsujishita, Hideki; Hori, Noriyuki; Ohishi, Yuichi; Inoue, Shintaro; Ikeda, Shoji; Okada, Yasunori

CS New Drug Discovery Research Laboratory, Kanebo Ltd., Osaka, 534, Japan

SO Journal of Medicinal Chemistry (1998), 41(8), 1209-1217

CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

IT **188728-61-2P 188728-67-8P**

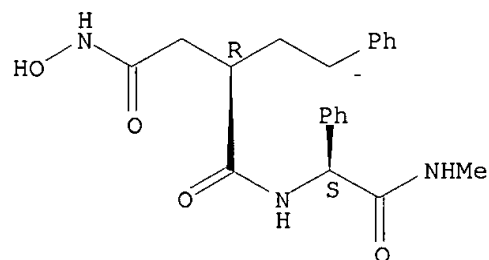
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. and biol. activity of hydroxamate inhibitors of matrix metalloproteinases)

RN 188728-61-2 CAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-2-(methylamino)-2-oxo-1-phenylethyl]-2-(2-phenylethyl)-, (2R)- (9CI) (CA INDEX NAME)

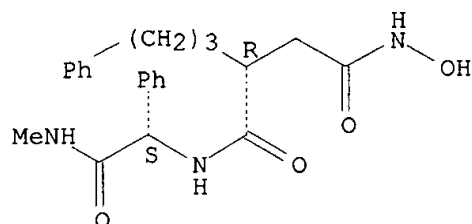
Absolute stereochemistry.



RN 188728-67-8 CAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-2-(methylamino)-2-oxo-1-phenylethyl]-2-(3-phenylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



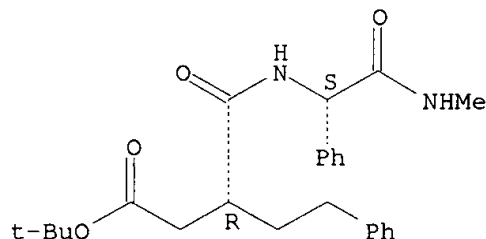
IT 188729-03-5P 188729-04-6P 205526-94-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and biol. activity of hydroxamate inhibitors of matrix metalloproteinases)

RN 188729-03-5 CAPLUS

CN Benzenepentanoic acid, .beta.-[[[2-(methylamino)-2-oxo-1-phenylethyl]amino]carbonyl]-, 1,1-dimethylethyl ester, [S-(R\*,S\*)]- (9CI)  
(CA INDEX NAME)

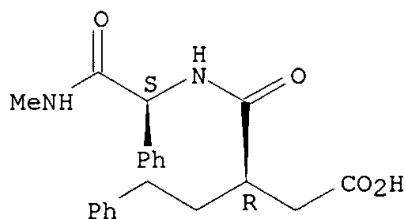
Absolute stereochemistry.



RN 188729-04-6 CAPLUS

CN Benzenepentanoic acid, .beta.-[[[2-(methylamino)-2-oxo-1-phenylethyl]amino]carbonyl]-, [S-(R\*,S\*)]- (9CI) (CA INDEX NAME)

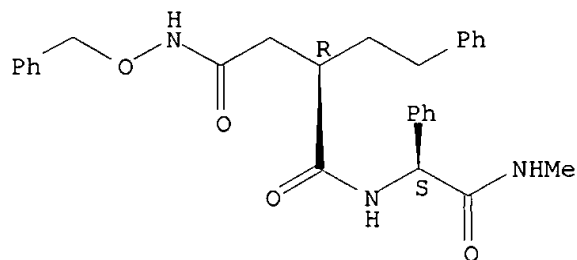
Absolute stereochemistry.



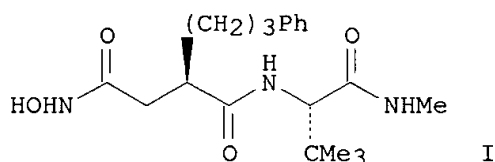
RN 205526-94-9 CAPLUS

CN Butanediamide, N1-[2-(methylamino)-2-oxo-1-phenylethyl]-2-(2-phenylethyl)-N4-(phenylmethoxy)-, [S-(R\*,S\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB The membrane-type 1 matrix metalloproteinase (MT1-MMP) has been reported to mediate the activation of pro-gelatinase A (proMMP-2), which is assocd. with tumor proliferation and metastasis. MT1-MMP can also digest extracellular matrix (ECM) such as interstitial collagens, gelatin, and proteoglycan and thus may play an important role in pathophysiol. digestion of ECM. The authors studied the inhibitory effect of various hydroxamate MMP inhibitors, including known inhibitors such as BB-94, BB-2516, GM6001, and Ro31-9790, on a deletion mutant of MT1-MMP lacking the transmembrane domain (.DELTA.MT1) to further characterize the enzyme and develop a selective inhibitor for MT1-MMP. The evaluation of the inhibitory activities of various hydroxamates reveals general structural profiles affecting selectivities toward MMPs. In particular, a longer side chain at the P1' position is preferable for the binding to MMP-2, -3, and -9 and MT1-MMP. For the P2' position, an .alpha.-branched alkyl group is crit. for the binding toward .DELTA.MT1, while the introduction of a bulky group at the .alpha.-position of hydroxamic acid seems to diminish the activity against .DELTA.MT1. Summation of the data on the sensitivity of .DELTA.MT1 to various hydroxamate inhibitors indicates that (1) the vol. of the S1' subsite of .DELTA.MT1 is similar to that of MMP-2, -3, and -9, which is bigger than that of MMP-1, and (2) the S1 and S2' subsites are narrower than those in other MMPs. On the basis of these results, the hydroxamates with a P1' phenylpropyl and P2' .alpha.-branched alkyl group were synthesized and evaluated for inhibitory activity. Inhibitors, such as hydroxamate I, showed strong activity against .DELTA.MT1 (IC50 = 1.9 nM) over MMP-1 (IC50 = 21 nM), but no selectivity between .DELTA.MT1 and MMP-9 (IC50 = 1.3 nM). These results are explained using mol. modeling studies conducted on MT1-MMP.

L4 ANSWER 53 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1998:31296 CAPLUS

DN 128:75670

TI Preparation of amino acid thiadiazole amide MMP inhibitors

IN Mitchell, Mark A.; Schostarez, Heinrich J.; Maggiora, Linda L.; Lindberg, Thomas J.



PA Pharmacia and Upjohn Co., USA; Mitchell, Mark A.; Schostarez, Heinrich J.;  
Maggiore, Linda L.; Lindberg, Thomas J.

SO PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.  | DATE     |
|----|---|------|----------|--|----------|
| PI | WO 9748688  | A1   | 19971224 | WO 1997-US9204   | 19970618 |
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|    | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, |      |          |  |          |
|    | DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, |      |          |  |          |
|    | LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, |      |          |  |          |
|    | PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, |      |          |  |          |
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|    | GN, ML, MR, NE, SN, TD, TG                                      |      |          |  |          |
|    |   |      |          | US 1996-20188P P   | 19960621 |
|    | AU 9734747  | A1   | 19980107 | AU 1997-34747  | 19970618 |
|    |   |      |          | US 1996-20188P P   | 19960621 |
|    |   |      |          | WO 1997-US9204 W   | 19970618 |
|    | EP 1021424  | A1   | 20000726 | EP 1997-931009   | 19970618 |
|    | EP 1021424  | B1   | 20030226 |  |          |
|    | R:  |      |          | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI |          |
|    |   |      |          | US 1996-20188P P   | 19960621 |
|    |   |      |          | WO 1997-US9204 W   | 19970618 |
|    | JP 2000514787   | T2   | 20001107 | JP 1998-503000   | 19970618 |
|    |   |      |          | US 1996-20188P P   | 19960621 |
|    |   |      |          | WO 1997-US9204 W   | 19970618 |
|    | AT 233251   | E    | 20030315 | AT 1997-931009   | 19970618 |
|    |   |      |          | US 1996-20188P P   | 19960621 |
|    |   |      |          | WO 1997-US9204 W   | 19970618 |

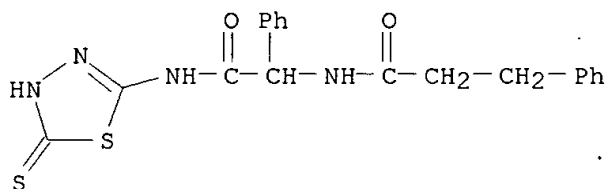
OS MARPAT 128:75670

IT **200642-32-6P 200642-33-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of amino acid thiadiazole amide MMP inhibitors)

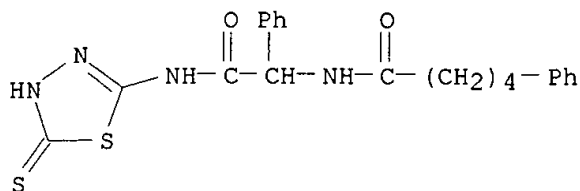
RN 200642-32-6 CAPLUS

CN Benzenepropanamide, N-[2-[(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)amino]-2-oxo-1-phenylethyl]- (9CI) (CA INDEX NAME)

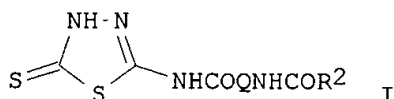


RN 200642-33-7 CAPLUS

CN Benzenepentanamide, N-[2-[(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)amino]-2-oxo-1-phenylethyl]- (9CI) (CA INDEX NAME)



GI



AB Amino acid thiadiazole amides I [Q = (CHR<sub>1</sub>)<sub>n</sub> (R<sub>1</sub> = H, alkyl, Ph, alkylaryl, cycloalkylalkyl, etc. and n = 1 or 2), C3-C6 1,2-cycloalkanediyl; R<sub>2</sub> = alkyl, arylalkyl, 3-indolylalkyl, 9H-fluoren-9-ylmethoxy, alkoxy, alkoxyalkyl, etc. ] were prepd. as MMP inhibitors. Thus, [2-[(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)amino]-2-oxo-1-phenylethyl]carbamic acid phenylmethyl ester was prepd. by coupling of 5-amino-1,3,4-thiadiazole-2-thione with Cbz-(+/-)-phenylglycine. The product was tested for inhibition of stromelysin (K<sub>i</sub> = 1,21 .mu.M).

L4 ANSWER 54 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1997:761604 CAPLUS

DN 128:30398

TI Agonist peptides of thrombin receptor and stimulation of platelet aggregation

IN Coughlin, Shaun R.; Scarborough, Robert M.

PA COR Therapeutics, Inc., USA

SO U.S., 89 pp., Cont.-in-part of U.S. 5,256,766.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.   | DATE     |
|----|---|------|----------|-------------------|----------|
| PI | US 5688768  | A    | 19971118 | US 1991-789184    | 19911107 |
|    |   |      |          | US 1991-657769 A2 | 19910219 |
|    | US 5256766  | A    | 19931026 | US 1991-657769    | 19910219 |
|    | CA 2104394  | AA   | 19920820 | CA 1992-2104394   | 19920219 |
|    |   |      |          | US 1991-657769 A  | 19910219 |
|    | WO 9214750  | A1   | 19920903 | WO 1992-US1312    | 19920219 |
|    | W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE |      |          |                   |          |
|    | RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG        |      |          |                   |          |
|    |   |      |          | US 1991-657769 A  | 19910219 |
|    |   |      |          | US 1991-789184 A  | 19911107 |
|    | AU 9214568  | A1   | 19920915 | AU 1992-14568     | 19920219 |

AU 665752 B2 19960118

EP 572553 A1 19931208

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE

JP 06508742 T2 19941006

US 6197541 B1 20010306

US 5759994 A 19980602

US 5798248 A 19980825

US 5849507 A 19981215

US 5856448 A 19990105

US 6024936 A 20000215

US 1991-657769 A 19910219

US 1991-789184 A 19911107

WO 1992-US1312 A 19920219

EP 1992-907700 19920219

US 1991-657769 A 19910219

US 1991-789184 A 19911107

WO 1992-US1312 W 19920219

JP 1992-507331 19920219

US 1991-657769 A 19910219

US 1991-789184 A 19911107

WO 1992-US1312 W 19920219

US 1993-18760 19930217

US 1991-657769 A119910219

US 1991-789184 A319911107

US 1995-475263 19950607

US 1991-657769 A219910219

US 1991-789184 A119911107

US 1995-485886 19950607

US 1991-657769 A219910219

US 1991-789184 A319911107

US 1995-477362 19950607

US 1991-657769 A219910219

US 1991-789184 A319911107

US 1995-477134 19950607

US 1991-657769 A219910219

US 1991-789184 A319911107

US 1995-473489 19950607

US 1991-657769 A219910219

US 1991-789184 A319911107

## PATENT FAMILY INFORMATION:

FAN 1993:116751

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.   | DATE     |
|----|---|------|----------|-------------------|----------|
| PI | WO 9214750  | A1   | 19920903 | WO 1992-US1312    | 19920219 |
|    | W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE |      |          |                   |          |
|    | RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG        |      |          |                   |          |
|    |   |      |          | US 1991-657769 A  | 19910219 |
|    |   |      |          | US 1991-789184 A  | 19911107 |
|    | US 5256766  | A    | 19931026 | US 1991-657769    | 19910219 |
|    | US 5688768  | A    | 19971118 | US 1991-789184    | 19911107 |
|    |   |      |          | US 1991-657769 A2 | 19910219 |
|    | AU 9214568  | A1   | 19920915 | AU 1992-14568     | 19920219 |
|    | AU 665752   | B2   | 19960118 |                   |          |
|    |   |      |          | US 1991-657769 A  | 19910219 |
|    |   |      |          | US 1991-789184 A  | 19911107 |
|    |   |      |          | WO 1992-US1312 A  | 19920219 |
|    | EP 572553   | A1   | 19931208 | EP 1992-907700    | 19920219 |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE   |      |          |                   |          |
|    |   |      |          | US 1991-657769 A  | 19910219 |
|    |   |      |          | US 1991-789184 A  | 19911107 |
|    |   |      |          | WO 1992-US1312 W  | 19920219 |
|    | JP 06508742   | T2   | 19941006 | JP 1992-507331    | 19920219 |
|    |   |      |          | US 1991-657769 A  | 19910219 |

US 1991-789184 A 19911107  
WO 1992-US1312 W 19920219

OS MARPAT 128:30398

IT **145229-80-7P 145230-57-5P**

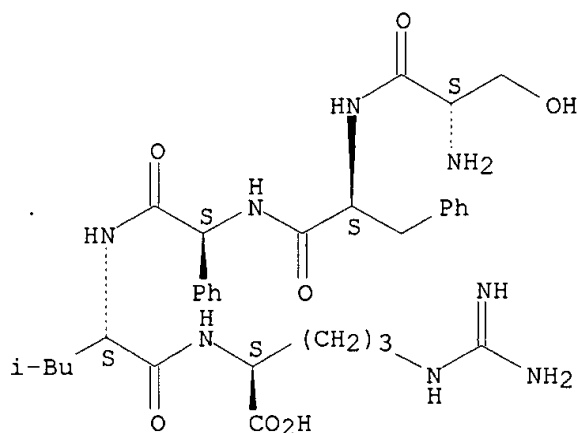
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(agonist peptides of thrombin receptor and stimulation of platelet aggregation)

RN 145229-80-7 CAPLUS

CN L-Arginine, L-seryl-L-phenylalanyl-(2S)-2-phenylglycyl-L-leucyl- (9CI)  
(CA INDEX NAME)

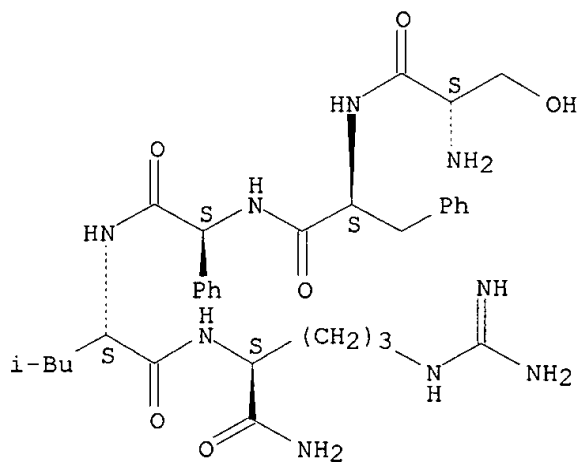
Absolute stereochemistry.



RN 145230-57-5 CAPLUS

CN L-Argininamide, L-seryl-L-phenylalanyl-(2S)-2-phenylglycyl-L-leucyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



AB Peptide agonists of the thrombin receptor which are useful for platelet

aggregation are claimed. CDNA encoding the human cell surface receptor for thrombin was cloned and sequenced. Peptides based on the N-terminus of the activated human thrombin receptor were prepd. and tested for agonist activity in platelet aggregation assays. Peptides with EC50's as low as 1.1 .mu.M were produced. Addnl., antagonist peptides, thrombin mutant antagonists, and anti-receptor antibody antagonists were prepd. and tested.

L4 ANSWER 55 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1997:643193 CAPLUS

DN 127:307517

TI Preparation of enantiopure precursors for the vitamin E synthesis. A comparison of the asymmetric allylation of ketones and the Sharpless bishydroxylation

AU Tietze, Lutz F.; Gorlitzer, Jochen

CS Institut Organische Chemie, Georg-August-Universitat, Goettingen, D-37077, Germany

SO Synlett (1997), (9), 1049-1050

CODEN: SYNLES; ISSN: 0936-5214

PB Thieme

DT Journal

LA English

OS CASREACT 127:307517

IT **197297-78-2P**

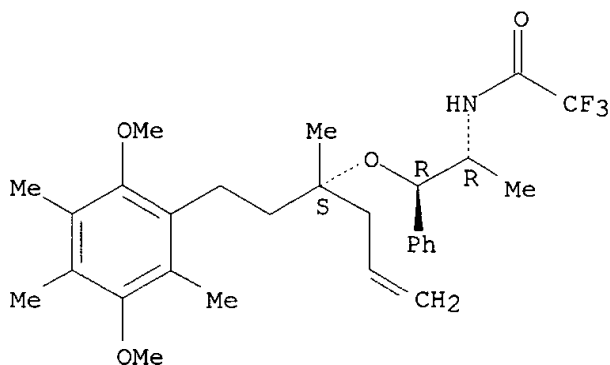
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of vitamin E precursors by asym. allylation of ketones and Sharpless bishydroxylation)

RN 197297-78-2 CAPLUS

CN Acetamide, N-[(1R,2R)-2-[[[(1S)-1-[2-(2,5-dimethoxy-3,4,6-trimethylphenyl)ethyl]-1-methyl-3-butenyl]oxy]-1-methyl-2-phenylethyl]-2,2,2-trifluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **197297-80-6P**

RL: SPN (Synthetic preparation); PREP (Preparation)

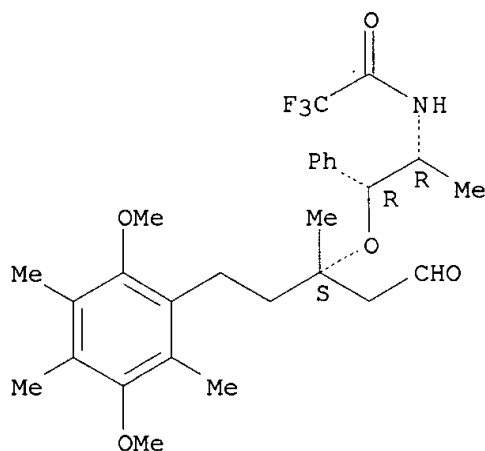
(synthesis of vitamin E precursors by asym. allylation of ketones and Sharpless bishydroxylation)

RN 197297-80-6 CAPLUS

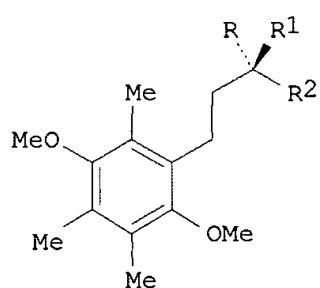
CN Acetamide, N-[(1R,2R)-2-[(S)-1-[2-(2,5-dimethoxy-3,4,6-trimethylphenyl)ethyl]-1-methyl-3-oxopropoxy]-1-methyl-2-phenylethyl]-

2,2,2-trifluoro- (9CI) (CA INDEX NAME)

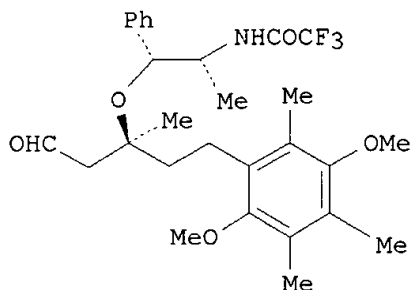
Absolute stereochemistry. Rotation (+).



GI



I



II

AB The enantioselective synthesis of the precursors I [R = OH, R1 = Me, R2 = allyl; R = Me, R1 = OH, R2 = CH<sub>2</sub>OH or (S)-CHOHCH<sub>2</sub>OH] and II for the prepn. of enantiopure .alpha.-tocopherol by asym. allylation of the ketone I (RR1 = O, R2 = Me) and Sharpless dihydroxylation of the aliph. alkenes I (RR1 = CH<sub>2</sub>, CHCH<sub>2</sub>OH; R2 = Me) is described.

L4 ANSWER 56 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1997:639948 CAPLUS

DN 127:307269

TI Preparation of optically active succinic acid derivatives. I. Optical resolution of 2-benzyl-3-(cis-hexahydroisoindolin-2-ylcarbonyl)propionic acid

AU Yamaguchi, Toshiaki; Yanagi, Takashi; Hokari, Hiroshi; Mukaiyama, Yuko; Kamijo, Tetsuhide; Yamamoto, Iwao

CS Kissei Pharmaceutical Co., Ltd., Central Research Laboratories, Hotaka, 399-83, Japan

SO Chemical & Pharmaceutical Bulletin (1997), 45(9), 1518-1520

CODEN: CPBTAL; ISSN: 0009-2363

PB Pharmaceutical Society of Japan

DT Journal

LA English

IT **197447-44-2P**

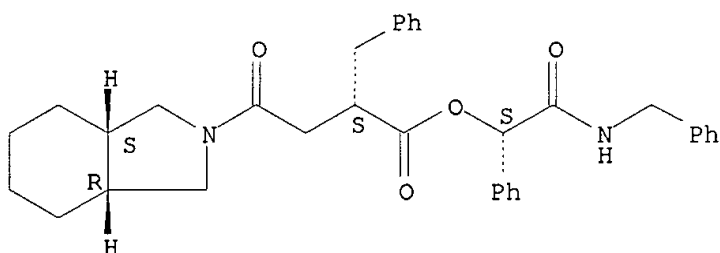
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(optical resolu. of benzyl(hexahydroisoindolinylicarbonyl)propionic acid)

RN 197447-44-2 CAPLUS

CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, 2-oxo-1-phenyl-2-[(phenylmethyl)amino]ethyl ester, [2(.alpha.S)-[2[R\*(R\*)],3a.alpha.,7a.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

IT **197447-45-3P**

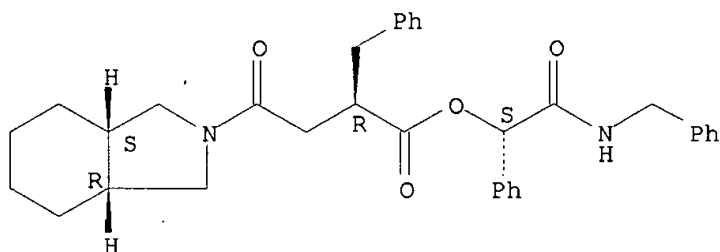
RL: SPN (Synthetic preparation); PREP (Preparation)

(optical resolu. of benzyl(hexahydroisoindolinylicarbonyl)propionic acid)

RN 197447-45-3 CAPLUS

CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, 2-oxo-1-phenyl-2-[(phenylmethyl)amino]ethyl ester, [2(.alpha.R)-[2[R\*(S\*)],3a.alpha.,7a.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB Optical resolu. of 2-benzyl-3-(cis-hexahydroisoindolin-2-ylcarbonyl)propionic acid (I) was accomplished by two methods. Thus, I was esterified with (S)-N-benzylmandelamide and the resulting diastereomeric esters were sepd. by column chromatog. on silica gel. One of the diastereomers was hydrolyzed to give the optically active acid (-)-I. The abs. configuration of (-)-I was established as S by comparison with an authentic sample. The alternative method was resolu. using an optically active amine. Treatment of a soln. of the racemic acid I with

0.65 equiv of (R)-1-(1-naphthyl)ethylamine in ethanol gave the salt in 23.2% yield with an optical purity of 96.8% ee.

L4 ANSWER 57 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1997:565204 CAPLUS

DN 127:248391

TI Synthesis of model tricyclic C-O-D-O-E-F-O-G ring of teicoplanin

AU Bois-Choussy, Michele; Vergne, Caroline; Neuville, Luc; Beugelmans, Rene; Zhu, Jieping

CS Inst. Chimie Substances Naturelles, Gif-sur-Yvette, 91198, Fr.

SO Tetrahedron Letters (1997), 38(33), 5795-5798

CODEN: TELEAY; ISSN: 0040-4039

PB Elsevier

DT Journal

LA English

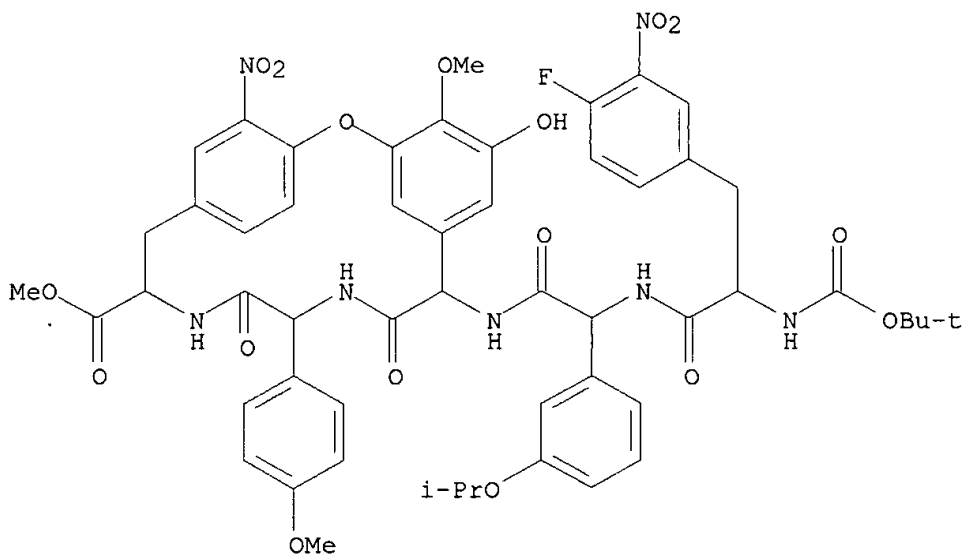
IT 195608-30-1P 195738-64-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of model tricyclic C-O-D-O-E-F-O-G ring of teicoplanin)

RN 195608-30-1 CAPLUS

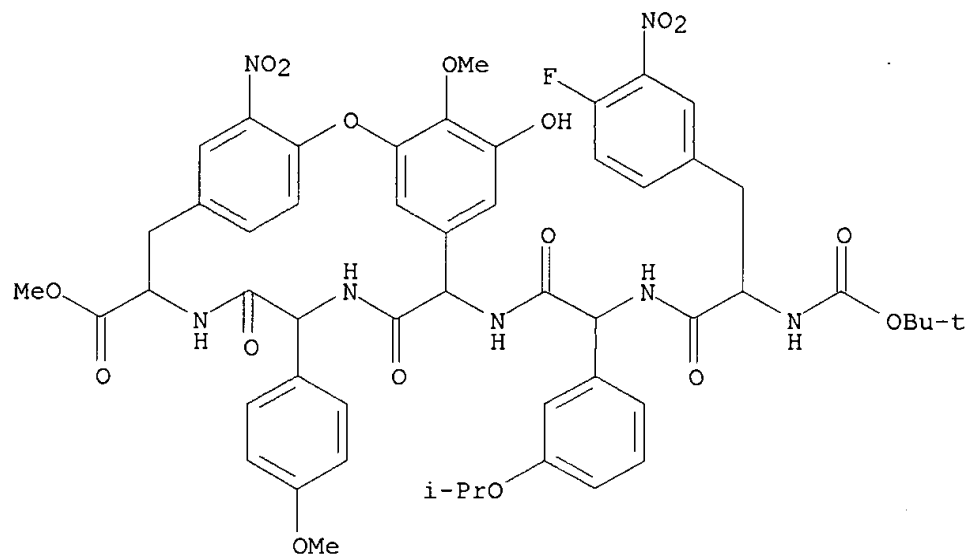
CN L-Tyrosine, N-[(1,1-dimethylethoxy)carbonyl]-4-fluoro-3-nitro-D-phenylalanyl-(2S)-2-[3-(1-methylethoxy)phenyl]glycyl-(2R)-2-(3,5-dihydroxy-4-methoxyphenyl)glycyl-(2R)-2-(4-methoxyphenyl)glycyl-3-nitro-, methyl ester, cyclic (3.fwdarw.5)-ether, stereoisomer (9CI) (CA INDEX NAME)



RN 195738-64-8 CAPLUS

CN L-Tyrosine, N-[(1,1-dimethylethoxy)carbonyl]-4-fluoro-3-nitro-D-phenylalanyl-(2S)-2-[3-(1-methylethoxy)phenyl]glycyl-(2R)-2-(3,5-dihydroxy-4-methoxyphenyl)glycyl-(2R)-2-(4-methoxyphenyl)glycyl-3-nitro-, methyl ester, cyclic (3.fwdarw.5)-ether, stereoisomer (9CI) (CA INDEX NAME)





AB    Synthesis of model tricyclic C-O-D-O-E-F-O-G rings of teicoplanin by means of efficient SNAr based cycloetherification methodol. is reported.

L4 ANSWER 58 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1997:547277 CAPLUS

DN 127:162122

TI Preparation of 5-amino-4-hydroxyhexanoic acid derivatives for treatment of AIDS

IN    **Bold, Guido; Lang, Marc; Fassler, Alexander; Capraro, Hans-georg; Bhagwat, Shripad; Schneider, Peter; Hoogevast, Peter**van

PA Ciba-Geigy Corp., USA

SO U.S., 98 pp., Cont.-in-part of U.S. Ser. No. 941,595, abandoned.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | US 5643878 | A    | 19970701 | US 1994-207646  | 19940308 |
|    |            |      |          | CH 1991-2689    | 19910912 |
|    |            |      |          | CH 1992-890     | 19920327 |
|    |            |      |          | CH 1992-2007    | 19920625 |
|    |            |      |          | US 1992-941595  | 19920908 |
|    | ZA 9206938 | A    | 19940311 | CH 1992-772     | 19930311 |
|    |            |      |          | ZA 1992-6938    | 19920911 |
|    |            |      |          | CH 1991-2689    | 19910912 |
|    | CN 1089269 | A    | 19940713 | CN 1993-100044  | 19930104 |
|    |            |      |          | CH 1991-2689    | 19910912 |

## PATENT FAMILY INFORMATION:

FAN 1993:650508

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
|    | -----      | ---- | -----    | -----           | -----    |
| PI | EP 532466  | A2   | 19930317 | EP 1992-810678  | 19920903 |
|    | EP 532466  | A3   | 19930616 |                 |          |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE  
CH 1991-2689 19910912

|             |    |          |                 |          |
|-------------|----|----------|-----------------|----------|
|             |    |          | CH 1992-980     | 19920327 |
|             |    |          | CH 1992-2007    | 19920625 |
| JP 05230095 | A2 | 19930907 | JP 1992-238424  | 19920907 |
|             |    |          | CH 1991-2689    | 19910912 |
|             |    |          | CH 1992-980     | 19920327 |
|             |    |          | CH 1992-2007    | 19920625 |
| CA 2077948  | AA | 19930313 | CA 1992-2077948 | 19920910 |
|             |    |          | CH 1991-2689    | 19910912 |
|             |    |          | CH 1992-980     | 19920327 |
|             |    |          | CH 1992-2007    | 19920625 |
| AU 9222889  | A1 | 19930318 | AU 1992-22889   | 19920910 |
| AU 661018   | B2 | 19950713 |                 |          |
|             |    |          | CH 1991-2689    | 19910912 |
|             |    |          | CH 1992-980     | 19920327 |
|             |    |          | CH 1992-2007    | 19920625 |
| IL 103126   | A1 | 19970930 | IL 1992-103126  | 19920910 |
|             |    |          | CH 1991-2689    | 19910912 |
|             |    |          | CH 1992-980     | 19920327 |
|             |    |          | CH 1992-2007    | 19920625 |
| NO 9203533  | A  | 19930315 | NO 1992-3533    | 19920911 |
|             |    |          | CH 1991-2689    | 19910912 |
|             |    |          | CH 1992-980     | 19920327 |
|             |    |          | CH 1992-2007    | 19920625 |
| HU 63632    | A2 | 19930928 | HU 1992-2925    | 19920911 |
|             |    |          | CH 1991-2689    | 19910912 |
|             |    |          | CH 1992-980     | 19920327 |
|             |    |          | CH 1992-2007    | 19920625 |
| ZA 9206938  | A  | 19940311 | ZA 1992-6938    | 19920911 |
|             |    |          | CH 1991-2689    | 19910912 |
| PL 169969   | B1 | 19960930 | PL 1992-295905  | 19920911 |
|             |    |          | CH 1991-2689    | 19910912 |
|             |    |          | CH 1992-980     | 19920327 |
|             |    |          | CH 1992-2007    | 19920625 |
| RU 2067585  | C1 | 19961010 | RU 1992-5052915 | 19920911 |
|             |    |          | CH 1991-2689    | 19910912 |
|             |    |          | CH 1992-980     | 19920327 |
|             |    |          | CH 1992-2007    | 19920625 |
| CN 1089269  | A  | 19940713 | CN 1993-100044  | 19930104 |
|             |    |          | CH 1991-2689    | 19910912 |

OS MARPAT 127:162122

IT **165453-86-1P**

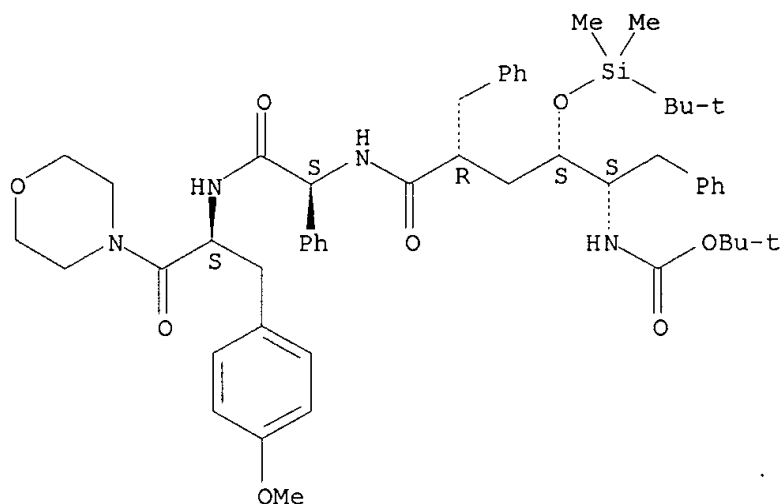
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of aminohydroxyhexanoic acid derivs. for treatment of AIDS)

RN 165453-86-1 CAPLUS

CN Carbamic acid, [2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-[[2-[[1-[(4-methoxyphenyl)methyl]-2-(4-morpholinyl)-2-oxoethyl]amino]-2-oxo-1-phenylethyl]amino]-5-oxo-1,4-bis(phenylmethyl)pentyl]-, 1,1-dimethylethyl ester, [1S-[1R\*,2R\*,4S\*,5[R\*(R\*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **165453-83-8P**

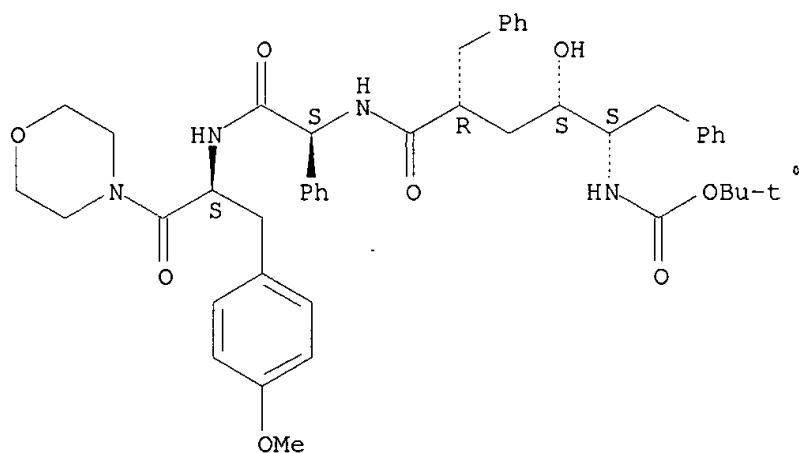
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of aminohydroxyhexanoic acid derivs. for treatment of AIDS)

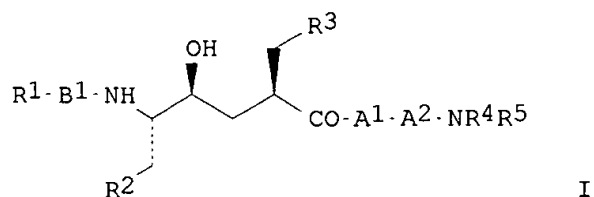
RN 165453-83-8 CAPLUS

CN Carbamic acid, [2-hydroxy-5-[[2-[[1-[(4-methoxyphenyl)methyl]-2-(4-morpholinyl)-2-oxoethyl]amino]-2-oxo-1-phenylethyl]amino]-5-oxo-1,4-bis(phenylmethyl)pentyl]-, 1,1-dimethylethyl ester, [1S-[1R\*,2R\*,4S\*,5[R\*(R\*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB Peptides I [A1, B1 = bond, amino acid residue; A2 = amino acid residue; R1 = H, alkoxycarbonyl, or (un)substituted benzyloxycarbonyl; R2, R3 = (un)substituted Ph or cyclohexyl; R4R5N = (un)substituted morpholino] were prepd. for the treatment of AIDS. Thus, 5(S)-Boc-amino-4(S)-hydroxy-6-cyclohexyl-2(R)-(p-fluorophenylmethyl)hexanoyl-L-Val-L-Phe-morpholin-4-ylamide (Boc = tert-butoxycarbonyl) was prepd. via peptide coupling in soln.

L4 ANSWER 59 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1997:348120 CAPLUS

DN 127:90113

TI Selective peptidic and peptidomimetic inhibitors of *Candida albicans* myristoylCoA:protein N-myristoyltransferase: a new approach to antifungal therapy

AU Sikorski, James A.; Devadas, Balekudru; Zupiec, Mark E.; Freeman, Sandra; Brown, David L.; Lu, Hwang-Fun; Nagarajan, Srinivasan; Mehta, Pramod P.; Wade, Arlene C.; Kishore, Nandini S.; Bryant, Martin L.; Getman, Daniel P.; McWherter, Charles A.; Gordon, Jeffrey I.

CS G. D. Searle Research and Development, Monsanto Company, St. Louis, MO, 63198, USA

SO Biopolymers (1997), 43(1), 43-71

CODEN: BIPMAA; ISSN: 0006-3525

PB Wiley

DT Journal

LA English

IT 190732-34-4

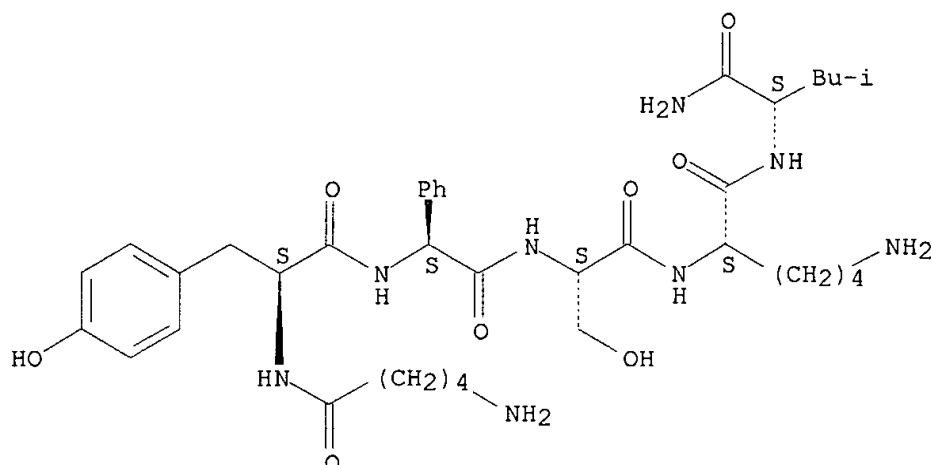
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(structure activity relations of inhibitors of *Candida albicans* myristoylCoA:protein N-myristoyltransferase and antifungal therapy)

RN 190732-34-4 CAPLUS

CN L-Leucinamide, N-(5-amino-1-oxopentyl)-L-tyrosyl-(2S)-2-phenylglycyl-L-seryl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

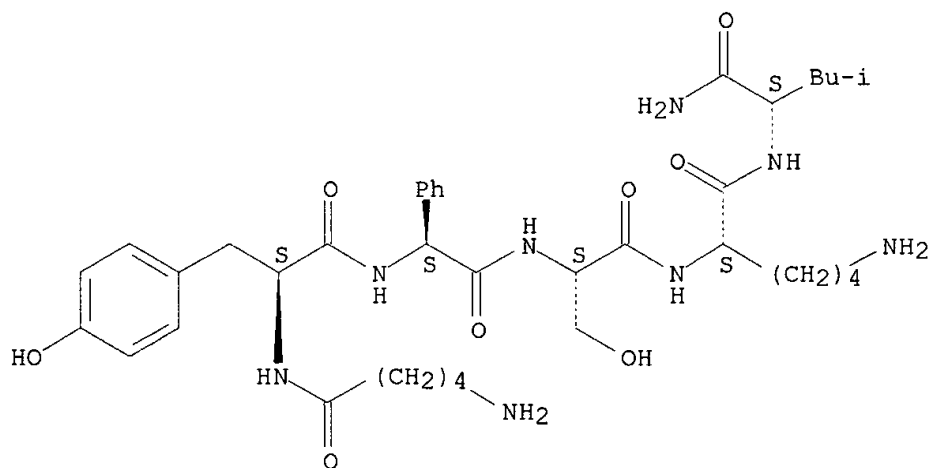


AB MyristoylCoA:protein N-myristoyltransferase (NMT) catalyzes the cotranslational covalent attachment of a rare cellular fatty acid, myristate, to the N-terminal Gly residue of a variety of eukaryotic proteins. The myristoyl moiety is often essential for expression of the biol. functions for these proteins. Attachment of C14:0 alone provides barely enough hydrophobicity to allow stable assocn. with membranes. The partitioning of N-myristoyl-proteins is therefore often modulated by "switches" that function through addnl. covalent or noncovalent modifications. *Candida albicans*, the principal cause of systemic fungal infection in immunocompromised humans, contains a single NMT gene that is essential for its viability. The functional properties of the acylCoA binding site of human and *C. albicans* NMT are very similar. However, there are distinct differences in their peptide binding sites. An ADP ribosylation factor (Arf) is included among the few cellular protein substrates of the fungal enzyme. Alanine scanning mutagenesis of an octapeptide derived from an N-terminal Arf sequence (GLYASKLS-NH<sub>2</sub>) disclosed that Gly1, Ser5, and Lys6 play predominant roles in binding. ALYASKLS-NH<sub>2</sub> is an inhibitor competitive for peptide [ $K_i(\text{app}) = 15.3 \pm 6.4 \mu\text{M}$ ] and noncompetitive for myristoylCoA. Remarkably, replacement of the N-terminal tetrapeptide with an 11-aminoundecanoyl group results in a competitive inhibitor (11-aminoundecanoyl-SKLS-NH<sub>2</sub>) that is approx. 40-fold more potent [ $K_i(\text{app}) = 0.40 \mu\text{M}$ ] than the starting octapeptide. Removal of Leu-Ser from the C-terminus generates a competitive dipeptide inhibitor (11-aminoundecanoyl-SK-NH<sub>2</sub>) with a  $K_i(\text{app})$  of 11.7  $\mu\text{M}$ , equiv. to that of the starting octapeptide. A deriv. dipeptide inhibitor contg. a C-terminal N-cyclohexylethyl lysinamide moiety has the advantage of being more potent ( $\text{IC}_{50} = 0.11 \mu\text{M}$ ) and resistant to digestion by cellular carboxypeptidases. Rigidifying the flexible aminoundecanoyl chain results in very potent general NMT inhibitors ( $\text{IC}_{50} = 40\text{--}50 \text{ nM}$ ). Substituting a 2-methyl-imidazole for the N-terminal amine and adding a benzylic  $\alpha$ -Me group with R stereochem. to the rigidifying element produces even more potent inhibitors ( $\text{IC}_{50} = 20\text{--}50 \text{ nM}$ ) that are up to 500-fold selective for the fungal compared to human enzyme. A related less potent member of this series of compds. is fungistatic. Its growth inhibitory effects are assocd. with a redn. in cellular protein N-myristoylation, judged using cellular Arf as a reporter. These studies establish that NMT is a new antifungal target.

L4 ANSWER 60 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1997:299761 CAPLUS  
 DN 127:30763  
 TI Scanning alanine mutagenesis and de-peptidization of a *Candida albicans* myristoyl-CoA:protein N-myristoyltransferase octapeptide substrate reveals three elements critical for molecular recognition  
 AU McWherter, Charles A.; Rocque, Warren J.; Zupec, Mark E.; Freeman, Sandra K.; Brown, David L.; Devadas, Balekudru; Getman, Daniel P.; Sikorski, James A.; Gordon, Jeffrey I.  
 CS Searle Discovery Res., Monsanto Co., St. Louis, MO, 63198, USA  
 SO Journal of Biological Chemistry (1997), 272(18), 11874-11880  
 CODEN: JBCHA3; ISSN: 0021-9258  
 PB American Society for Biochemistry and Molecular Biology  
 DT Journal  
 LA English  
 IT **190732-34-4**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (prepn. of inhibitors and identification of elements crit. for mol. recognition by *Candida albicans* myristoyl-CoA:protein N-myristoyltransferase by scanning alanine mutagenesis and de-peptidization of octapeptide substrate)  
 RN 190732-34-4 CAPLUS  
 CN L-Leucinamide, N-(5-amino-1-oxopentyl)-L-tyrosyl-(2S)-2-phenylglycyl-L-seryl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB *Candida albicans* produces a single myristoyl-CoA:protein N-myristoyltransferase (Nmt) that is essential for its viability. An ADP-ribosylation factor (Arf) is included among the few cellular protein substrates of this enzyme. An octapeptide (GLYASKLS-NH<sub>2</sub>) derived from a N-terminal Arf sequence was used as the starting point to identify elements crit. for recognition by the acyl-transferase's peptide-binding site. In vitro kinetic studies, employing purified Nmt and a panel of peptides with single Ala substitutions at each position of GLYASKLS-NH<sub>2</sub>, established that its Gly, Ser, and Lys residues play predominant roles in binding. ALYASKLS-NH<sub>2</sub> was found to be an inhibitor competitive for peptide ( $K_i = 15.3 \pm 6.4 \mu\text{M}$ ) and noncompetitive for myristoyl-CoA ( $K_i = 31.2 \pm 0.7 \mu\text{M}$ ). A survey of 26 derivs. of this inhibitor,

representing (i) a complete alanine scan, (ii) progressive C-terminal truncations, and (iii) manipulation of the phys.-chem. properties of its residues 1, 5, and 6, confirmed the important stereochem. requirements for the N-terminal amine, the .beta.-hydroxyl of Ser, and the .epsilon.-amino group of Lys. Remarkably, replacement of the N-terminal tetrapeptide of ALYASKLS-NH<sub>2</sub> with an 11-aminoundecanoyl group produced a competitive inhibitor, 11-aminoundecanoyl-SKLS-NH<sub>2</sub>, that was 38-fold more potent ( $K_i = 0.40 \pm 0.03 \mu\text{M}$ ) than the starting octapeptide. Removing the primary amine (undecanoyl-SKLS-NH<sub>2</sub>), or replacing it with a Me group (dodecanoyl-SKLS-NH<sub>2</sub>), resulted in 26- and 34-fold increases in IC<sub>50</sub>, confirming the important contribution of the amine to recognition. Removal of Leu-Ser from the C terminus (11-aminoundecanoyl-SK-NH<sub>2</sub>) yielded a competitive dipeptide inhibitor with a  $K_i$  ( $11.7 \pm 0.4 \mu\text{M}$ ) equiv. to that of the starting octapeptide, ALYASKLS-NH<sub>2</sub>. Substitution of Ser with homoserine, cis-4-hydroxyproline, or tyrosine reduces potency by 3-70-fold, emphasizing the requirement for proper presentation of the hydroxyl group in the dipeptide inhibitor. Substituting D- for L-Lys decreases its inhibitory activity >100-fold, while deletion of the .epsilon.-amino group (Nle) or masking its charge (.epsilon.-N-acetyllysine) produces 4-7-fold attenuations. L-His, but not its D-isomer, can fully substitute for L-Lys, producing a competitive dipeptide inhibitor with similar potency ( $K_i = 11.9 \pm 1.0 \mu\text{M}$ ). 11-Aminoundecanoyl-SK-NH<sub>2</sub> and 11-aminoundecanoyl-SH-NH<sub>2</sub> establish that a simple alkyl backbone can maintain an appropriate distance between three elements crit. for recognition by the fungal enzyme's peptide-binding site: a simple .omega.-terminal amino group, a .beta.-hydroxyl, and an .epsilon.-amino group or an imidazole. These compds. contain one peptide bond and two chiral centers, suggesting that it may be feasible to incorporate these elements of recognition, or functionally equiv. mimics, into a fully de-peptidized Nmt inhibitor.

L4 ANSWER 61 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1997:278955 CAPLUS

DN 126:264355

TI Preparation of N-containing compounds as Fas ligand solubilization inhibitors

IN Hirano, Takao; Yagita, Hideo; Okumura, Ko; Hirayama, Ryoichi; Yamamoto, Minoru; Ebata, Tomohiko; Ohmoto, Hiroshi; Ikeda, Shoji; Yoshino, Kohichiro

PA Kanebo, Ltd., Japan; Hirano, Takao; Yagita, Hideo; Okumura, Ko; Hirayama, Ryoichi; Yamamoto, Minoru; Ebata, Tomohiko; Ohmoto, Hiroshi; Ikeda, Shoji; Yoshino, Kohichiro

SO PCT Int. Appl., 123 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|----|--|------|----------|-----------------|----------|
| PI | WO 9709066   | A1   | 19970313 | WO 1996-JP2492  | 19960904 |
|    | W: CA, CN, KR, NO, US  |      |          |                 |          |
|    | RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE |      |          |                 |          |
|    |  |      |          | JP 1995-256897  | 19950908 |
|    |  |      |          | JP 1995-317136  | 19951109 |
|    | EP 848957  | A1   | 19980624 | EP 1996-929510  | 19960904 |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI  |      |          |                 |          |
|    |  |      |          | JP 1995-256897  | 19950908 |
|    |  |      |          | JP 1995-317136  | 19951109 |

|             |    |          |                |          |
|-------------|----|----------|----------------|----------|
|             |    |          | WO 1996-JP2492 | 19960904 |
| JP 09188631 | A2 | 19970722 | JP 1996-257868 | 19960906 |
|             |    |          | JP 1995-256897 | 19950908 |
|             |    |          | JP 1995-317136 | 19951109 |

OS MARPAT 126:264355

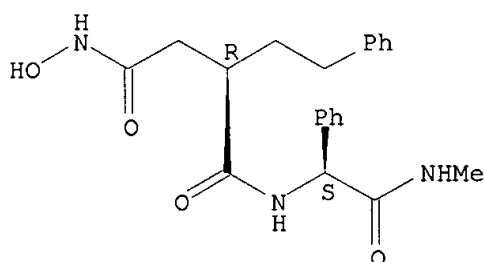
IT **188728-61-2P 188728-67-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of N-contg. compds. as Fas ligand solubilization inhibitors)

RN 188728-61-2 CAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-2-(methylamino)-2-oxo-1-phenylethyl]-2-(2-phenylethyl)-, (2R)- (9CI) (CA INDEX NAME)

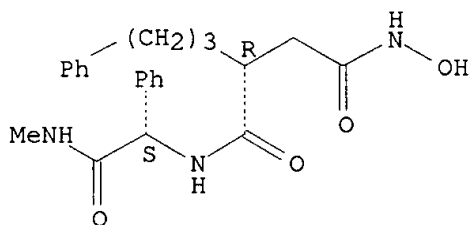
Absolute stereochemistry.



RN 188728-67-8 CAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-2-(methylamino)-2-oxo-1-phenylethyl]-2-(3-phenylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT **188729-03-5P 188729-04-6P 188729-09-1P****188729-10-4P**

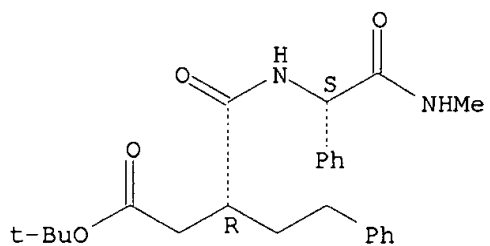
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of N-contg. compds. as Fas ligand solubilization inhibitors)

RN 188729-03-5 CAPLUS

CN Benzenepentanoic acid, .beta.-[[[2-(methylamino)-2-oxo-1-phenylethyl]amino]carbonyl]-, 1,1-dimethylethyl ester, [S-(R\*,S\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

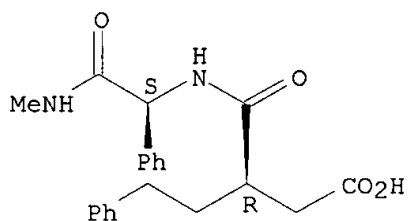




RN 188729-04-6 CAPLUS

CN Benzenepentanoic acid, .beta.-[[[2-(methylamino)-2-oxo-1-phenylethyl]amino]carbonyl]-, [S-(R\*,S\*)]- (9CI) (CA INDEX NAME)

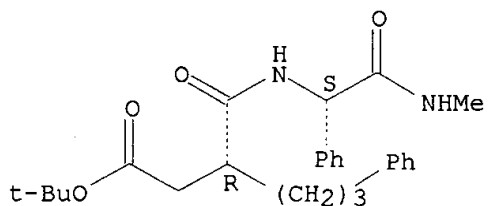
Absolute stereochemistry.



RN 188729-09-1 CAPLUS

CN Benzenhexanoic acid, .beta.-[[[2-(methylamino)-2-oxo-1-phenylethyl]amino]carbonyl]-, 1,1-dimethylethyl ester, [S-(R\*,S\*)]- (9CI) (CA INDEX NAME)

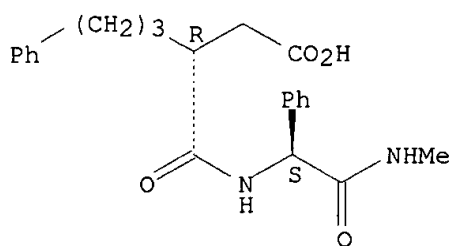
Absolute stereochemistry.



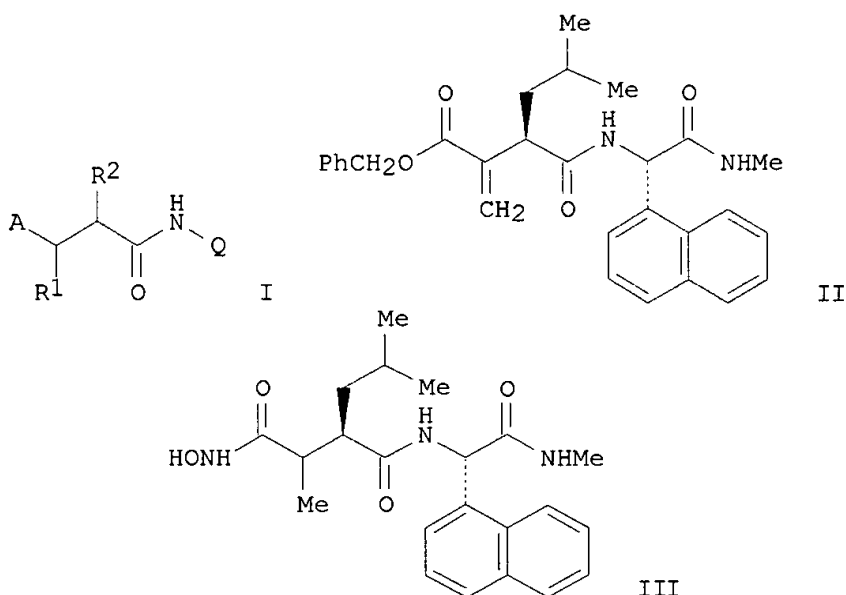
RN 188729-10-4 CAPLUS

CN Benzenhexanoic acid, .beta.-[[[2-(methylamino)-2-oxo-1-phenylethyl]amino]carbonyl]-, [S-(R\*,S\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



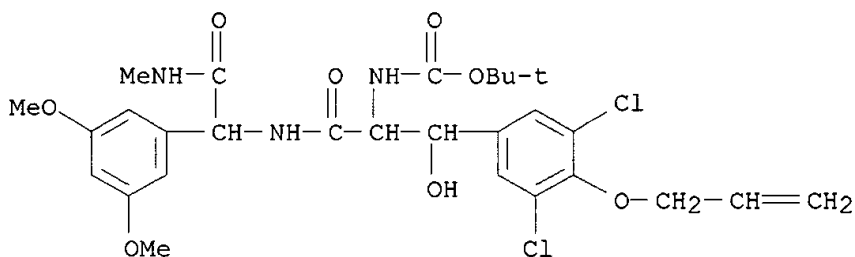
GI



AB The title compds. (I; A = N-hydroxyaminocarbonyl, CO<sub>2</sub>H, SH, etc.; R<sub>1</sub> = H, NH<sub>2</sub>, OH, SH, C<sub>1</sub>-6 alkoxy or alkyl, etc.; R<sub>2</sub> = H, C<sub>1</sub>-6 alkyl or alkylthio, C<sub>2</sub>-6 alkenyl, etc.; R<sub>3</sub> = C<sub>1</sub>-6 alkyl, C<sub>2</sub>-6 alkenyl, etc.; R<sub>4</sub> = H, C<sub>1</sub>-6 alkyl or alkoxy, etc.; R<sub>5</sub> = H, C<sub>1</sub>-6 alkyl, etc.; R<sub>6</sub> = H, OH, C<sub>1</sub>-6 alkoxy, etc.; R<sub>7</sub> = H, OH, OMe; n = 5-7) or pharmaceutically acceptable salts thereof are prepd. I, having a matrix metalloprotease inhibitory activity, are useful as Fas ligand solubilization inhibitors in the prevention or treatment of diseases caused by solubilized Fas ligands such as hepatitis, GVHD, AIDS, and autoimmune diseases. Thus, L-alanine deriv. (II) was hydrogenated over Pd/C, reacted with C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>ONH<sub>2</sub>.HCl in the presence of WSC, Et<sub>3</sub>N, and hydroxybenzotriazole, and then hydrogenated again over Pd/C to give the title compd. (III). III showed 50% Fas ligand secretion inhibitory when tested on mouse p.o.

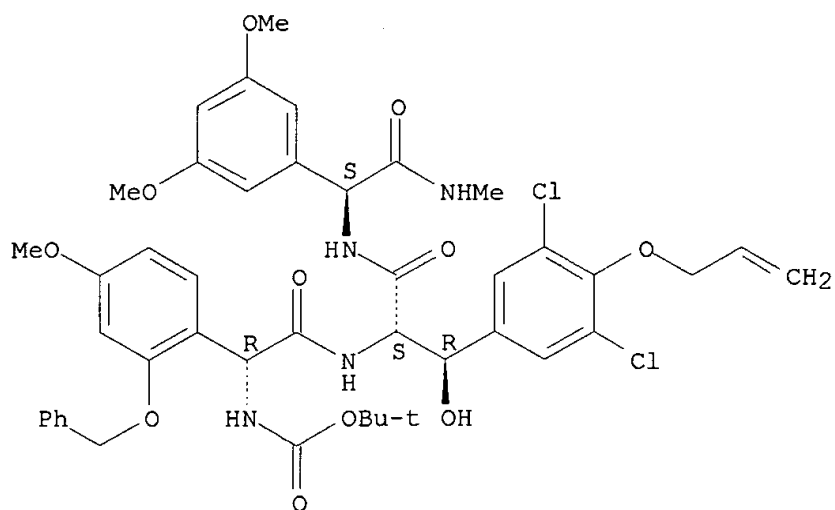
L4 ANSWER 62 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1997:196190 CAPLUS  
 DN 126:293596

TI Synthesis and Conformational Properties of the M(4-6) (5-7) Bicyclic  
Tetrapeptide Common to the Vancomycin Antibiotics  
AU Evans, David A.; Dinsmore, Christopher J.; Ratz, Andrew M.; Evrard,  
Deborah A.; Barrow, James C.  
CS Department of Chemistry and Chemical Biology, Harvard University,  
Cambridge, MA, 02138, USA  
SO Journal of the American Chemical Society (1997), 119(14), 3417-3418  
CODEN: JACSAT; ISSN: 0002-7863  
PB American Chemical Society  
DT Journal  
LA English  
OS CASREACT 126:293596  
IT **149623-65-4**  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. and conformational properties of bicyclic tetrapeptides common  
to vancomycin antibiotics)  
RN 149623-65-4 CAPLUS  
CN Glycinamide, (.beta.R)-3,5-dichloro-N-[(1,1-dimethylethoxy)carbonyl]-  
.beta.-hydroxy-O-2-propenyl-L-tyrosyl-(2S)-2-(3,5-dimethoxyphenyl)-N-  
methyl- (9CI) (CA INDEX NAME)



IT **189005-38-7P 189005-39-8P 189005-40-1P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. and conformational properties of bicyclic tetrapeptides common  
to vancomycin antibiotics)  
RN 189005-38-7 CAPLUS  
CN Glycinamide, (2R)-N-[(1,1-dimethylethoxy)carbonyl]-2-[4-methoxy-2-  
(phenylmethoxy)phenyl]glycyl-(.beta.R)-3,5-dichloro-.beta.-hydroxy-O-2-  
propenyl-L-tyrosyl-2-(3,5-dimethoxyphenyl)-N-methyl-, (2S)- (9CI) (CA  
INDEX NAME)

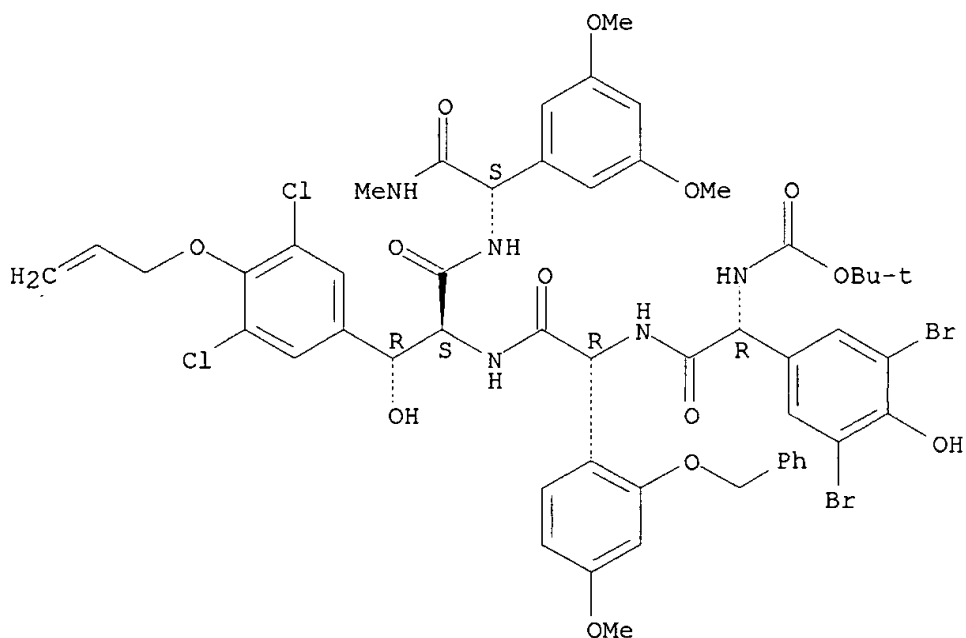
Absolute stereochemistry.



RN 189005-39-8 CAPLUS

CN Glycinamide, (2R)-2-(3,5-dibromo-4-hydroxyphenyl)-N-[(1,1-dimethylethoxy)carbonyl]glycyl-(2R)-2-[4-methoxy-2-(phenylmethoxy)phenyl]glycyl-(.beta.R)-3,5-dichloro-.beta.-hydroxy-O-2-propenyl-L-tyrosyl-2-(3,5-dimethoxyphenyl)-N-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

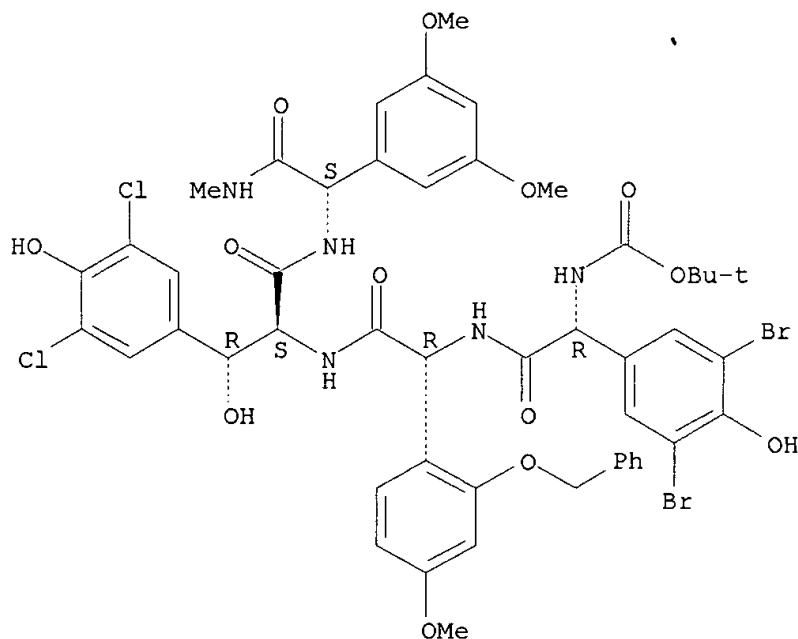


RN 189005-40-1 CAPLUS

CN Glycinamide, (2R)-2-(3,5-dibromo-4-hydroxyphenyl)-N-[(1,1-

dimethylethoxy)carbonyl]glycyl-(2R)-2-[4-methoxy-2-(phenylmethoxy)phenyl]glycyl-(.beta.R)-3,5-dichloro-.beta.-hydroxy-L-tyrosyl-2-(3,5-dimethoxyphenyl)-N-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The prepn. and conformational anal. of fully functionalized vancomycin M(4-6) (5-7) tetrapeptide (S)-atropisomer I (R = CH<sub>2</sub>Ph; R<sub>1</sub> = CO<sub>2</sub>CMe<sub>3</sub>, R<sub>2</sub> = R<sub>4</sub> = H, R<sub>3</sub> = iodo) is described. The key step involves oxidative biaryl cyclization of monocyclic tetrapeptide II with VOF<sub>3</sub>, BF<sub>3</sub>.OEt<sub>2</sub>, AgBF<sub>4</sub>, and CF<sub>3</sub>CO<sub>2</sub>H to give highly strained, unnatural (R)-atropisomer I (R = Me, R<sub>1</sub> = COCF<sub>3</sub>, R<sub>2</sub> = SO<sub>2</sub>Me, R<sub>3</sub> = Br, R<sub>4</sub> = OH). The ring 5 phenol was removed conversion to the triflate followed by reductive cleavage, and removal of the Me ether protecting groups from rings 5 and 7 was followed by atropisomerization to give (S)-atropisomer I (R = R<sub>3</sub> = R<sub>4</sub> = H, R<sub>1</sub> = COCF<sub>3</sub>, R<sub>2</sub> = SO<sub>2</sub>Me) as a single stereoisomer. Conformational properties of I (R = R<sub>3</sub> = R<sub>4</sub> = H, R<sub>1</sub> = COCF<sub>3</sub>, R<sub>2</sub> = SO<sub>2</sub>Me) and related biaryl tetrapeptides and tripeptides shows that the M(4-6) macrocycle has a profound influence on the kinetic and thermodyn. stability of the atropisomers. The presence of the M(4-6) macrocycle reinforces both the stability of the (S) biaryl atropisomer (>98:2) and the bias for the cis configuration of the (5-6) amide bond found in the natural vancomycin structure.

L4 ANSWER 63 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1997:105321 CAPLUS  
DN 126:118205  
TI Preparation of 5-amino-1,3,4-thiadiazone amino acid and peptide amides as  
inhibitors for matrix metalloproteinases  
IN Oleksyszyn, Josef; Jacobson, Alan R.  
PA Osteoarthritis Sciences, Inc., USA; Oleksyszyn, Josef; Jacobson, Alan R.  
SO PCT Int. Appl., 68 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

|    | PATENT NO.  | KIND   | DATE     | APPLICATION NO.  | DATE     |
|----|-------------|--|----------|------------------|----------|
| PI | WO 9640745  | A2   | 19961219 | WO 1996-US9095   | 19960606 |
|    | WO 9640745  | A3   | 19970130 |                  |          |
|    | W:          | AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG |          |                  |          |
|    | RW:         | KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA   |          |                  |          |
|    |             |  |          | US 1995-473143 A | 19950607 |
|    | US 5677282  | A  | 19971014 | US 1995-473143   | 19950607 |
|    | CA 2224113  | AA   | 19961219 | CA 1996-2224113  | 19960606 |
|    |             |  |          | US 1995-473143 A | 19950607 |
|    | AU 9660496  | A1   | 19961230 | AU 1996-60496    | 19960606 |
|    |             |  |          | US 1995-473143 A | 19950607 |
|    |             |  |          | WO 1996-US9095 W | 19960606 |
|    | EP 845002   | A2   | 19980603 | EP 1996-918174   | 19960606 |
|    | R:          | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI   |          |                  |          |
|    |             |  |          | US 1995-473143 A | 19950607 |
|    |             |  |          | WO 1996-US9095 W | 19960606 |
|    | JP 11506784 | T2   | 19990615 | JP 1996-501497   | 19960606 |
|    |             |  |          | US 1995-473143 A | 19950607 |
|    |             |  |          | WO 1996-US9095 W | 19960606 |
|    | ZA 9604830  | A  | 19970609 | ZA 1996-4830     | 19960607 |
|    |             |  |          | US 1995-473143 A | 19950607 |

OS MARPAT 126:118205

IT **186098-36-2P**

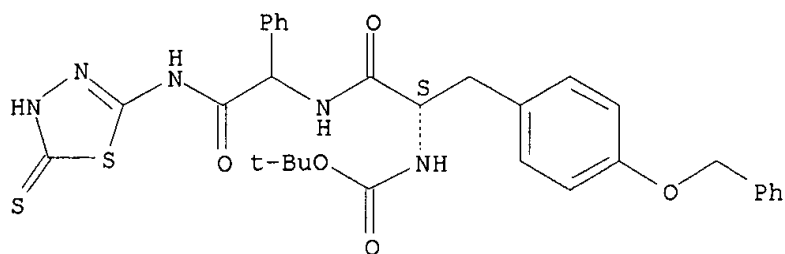
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of aminothiadiazoethione amino acid and peptide amides as matrix metalloproteinase inhibitors)

RN 186098-36-2 CAPLUS

CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



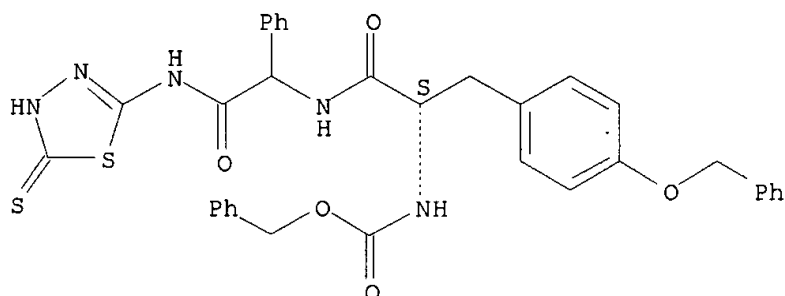
IT 186097-89-2P 186098-00-0P 186098-04-4P  
186098-07-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of aminothiadiazoethione amino acid and peptide amides as matrix metalloproteinase inhibitors)

RN 186097-89-2 CAPLUS

CN Glycinamide, N-[(phenylmethoxy)carbonyl]-O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl- (9CI) (CA INDEX NAME)

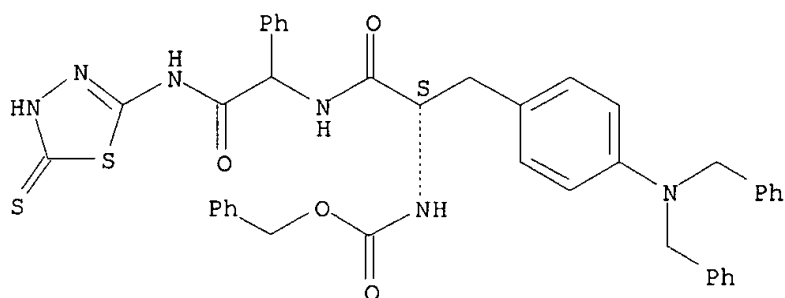
Absolute stereochemistry.



RN 186098-00-0 CAPLUS

CN Glycinamide, 4-[bis(phenylmethyl)amino]-N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

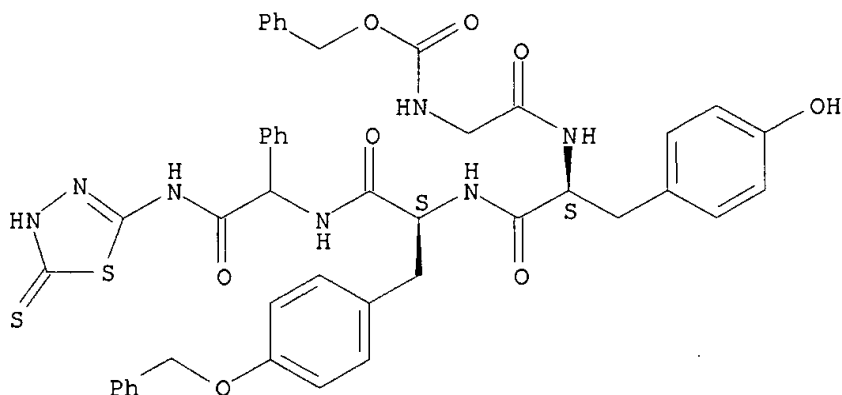


RN 186098-04-4 CAPLUS

CN Glycinamide, N-[(phenylmethoxy)carbonyl]glycyl-L-tyrosyl-O-(phenylmethyl)-

L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl- (9CI)  
(CA INDEX NAME)

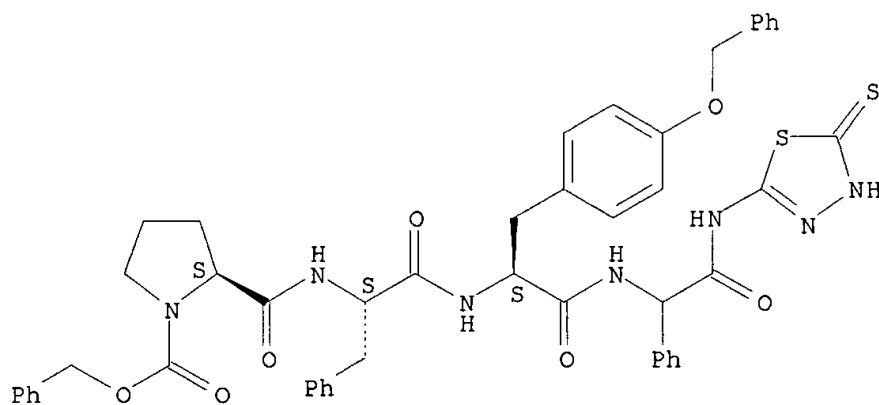
Absolute stereochemistry.



RN 186098-07-7 CAPLUS

CN Glycinamide, 1-[(phenylmethoxy)carbonyl]-L-prolyl-L-phenylalanyl-O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 186098-66-8 186098-67-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

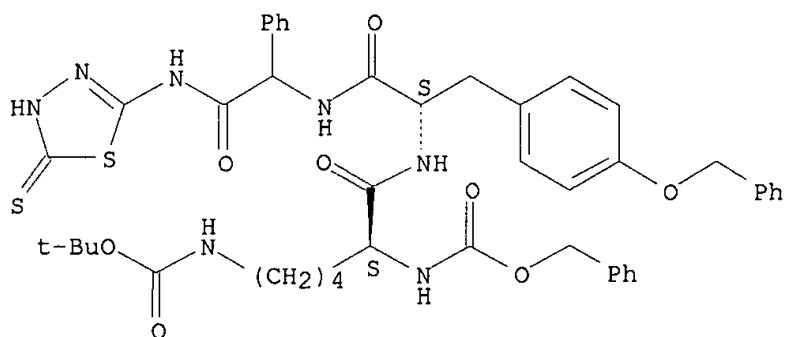
(prepn. of aminothiadiazoethione amino acid and peptide amides as matrix metalloproteinase inhibitors)

RN 186098-66-8 CAPLUS

CN Glycinamide, N6-[(1,1-dimethylethoxy)carbonyl]-N2-[(phenylmethoxy)carbonyl]-L-lysyl-O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

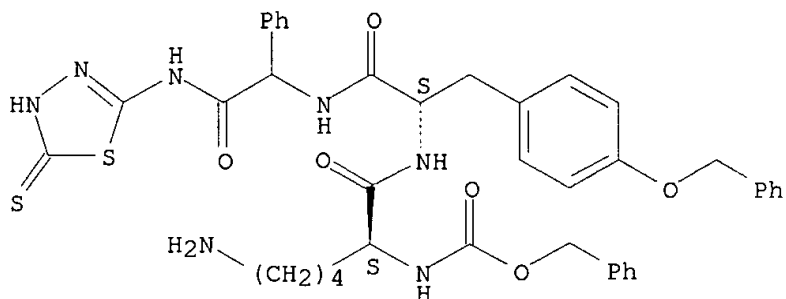




RN 186098-67-9 CAPLUS

CN Glycinamide, N2-[(phenylmethoxy)carbonyl]-L-lysyl-O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



IT 186098-37-3P

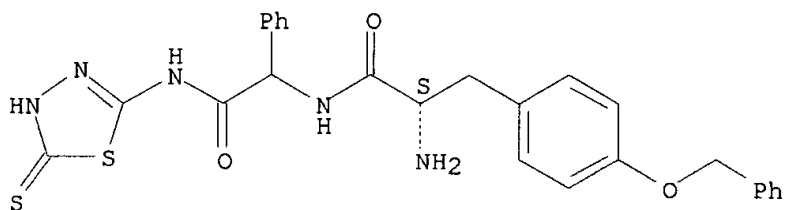
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of aminothiadiazoethione amino acid and peptide amides as matrix metalloproteinase inhibitors)

RN 186098-37-3 CAPLUS

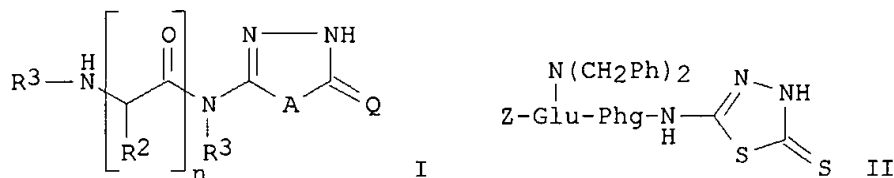
CN Glycinamide, O-(phenylmethyl)-L-tyrosyl-N-(4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl)-2-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HCl

GI



AB Title amino acid and peptide amides I [Q, A = independently S, O, with at least one Q, A being S; n = pos. integer; R1 = H, lower alkyl, acyl; each R2 = independently (un)substituted C1-10 straight or branched alkyl, C3-8 cycloalkyl, C1-10 straight or branched alkenyl, C1-10 straight or branched alkynyl; aryl, heteroaryl; R3 = amine protecting group, physiol. active salt] are disclosed. These compds. inhibit matrix metalloproteinase enzymes and cartilage degrading. Methods of treating diseases caused by over-activity of matrix metalloproteinases, such as osteoarthritis and rheumatoid arthritis, are also disclosed. Thus, coupling of Z-Glu[N(CH<sub>2</sub>Ph)<sub>2</sub>]-Phg-OH (Z = PhCH<sub>2</sub>O<sub>2</sub>C; Phg = phenylglycine) with 5-amino-1,3,4-thiadiazole-2-thiol gave peptide thiadiazolylamide II. II inhibited stromelysin with K<sub>i</sub> = 19 nM in a competitive inhibition assay.

L4 ANSWER 64 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1997:9227 CAPLUS

DN 126:31668

TI Preparation of cyclic pentapeptide LH-RH receptor antagonists

IN Kitada, Chieko; Furuya, Shuichi; Kato, Koichi

PA Takeda Chemical Industries, Ltd., Japan; Kitada, Chieko; Furuya, Shuichi; Kato, Koichi

SO PCT Int. Appl., 199 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.  | DATE     |
|----|---|------|----------|------------------|----------|
| PI | WO 9634012  | A1   | 19961031 | WO 1996-JP1140   | 19960425 |
|    | W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU |      |          |                  |          |
|    | RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG  |      |          |                  |          |
|    |   |      |          | JP 1995-106775 A | 19950428 |
|    |   |      |          | JP 1995-110933 A | 19950509 |
| CA | 2215737   | AA   | 19961031 | CA 1996-2215737  | 19960425 |
|    |   |      |          | JP 1995-106775 A | 19950428 |
|    |   |      |          | JP 1995-110933 A | 19950509 |
| AU | 9655143   | A1   | 19961118 | AU 1996-55143    | 19960425 |
|    |   |      |          | JP 1995-106775 A | 19950428 |
|    |   |      |          | JP 1995-110933 A | 19950509 |
|    |   |      |          | WO 1996-JP1140 W | 19960425 |
| EP | 822939  | A1   | 19980211 | EP 1996-912247   | 19960425 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI

|             |    |          |                  |          |
|-------------|----|----------|------------------|----------|
|             |    |          | JP 1995-106775 A | 19950428 |
|             |    |          | JP 1995-110933 A | 19950509 |
|             |    |          | WO 1996-JP1140 W | 19960425 |
| CN 1183104  | A  | 19980527 | CN 1996-193586   | 19960425 |
|             |    |          | JP 1995-106775 A | 19950428 |
|             |    |          | JP 1995-110933 A | 19950509 |
| JP 09025294 | A2 | 19970128 | JP 1996-107405   | 19960426 |
|             |    |          | JP 1995-106775 A | 19950428 |
|             |    |          | JP 1995-110933 A | 19950509 |
| US 6136781  | A  | 20001024 | US 1996-656244   | 19960606 |
|             |    |          | JP 1995-106775 A | 19950428 |
|             |    |          | JP 1995-110933 A | 19950509 |
|             |    |          | WO 1996-JP1140 W | 19960425 |

OS MARPAT 126:31668

IT **184836-92-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

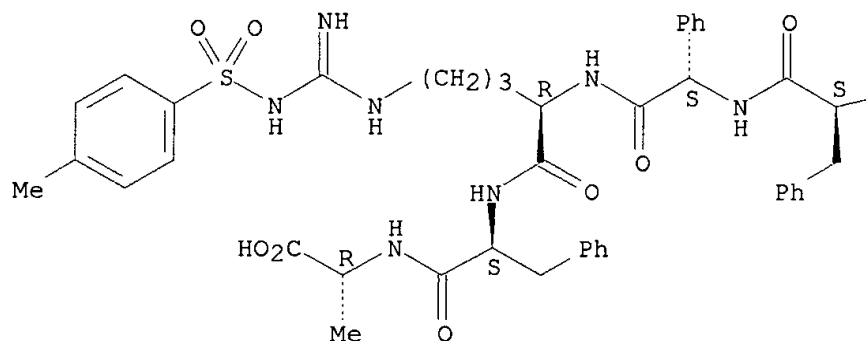
(prepn. of cyclic pentapeptide LH-RH receptor antagonists)

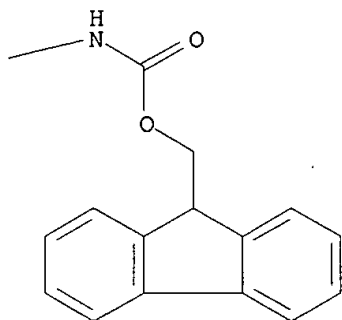
RN 184836-92-8 CAPLUS

CN D-Alanine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-phenylalanyl-(2S)-2-phenylglycyl-N5-[imino[[[4-methylphenyl)sulfonyl]amino]methyl]-D-ornithyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





AB LH-RH receptor antagonists contg. cyclic pentapeptides or salts thereof and novel cyclic pentapeptide or salts thereof are provided. These LH-RH receptor antagonists are effective as medicines for preventing and curing sex hormone-dependent cancers (e.g., prostatic cancer, uterine cancer, mammary cancer, pituitary tumor, etc.), prostatomegaly, endometriosis, hysterymyoma, puberty precox, amenorrheal syndromes, multilocular ovarian syndromes, comedo, etc, and are also effective as pregnancy controlling agents (e.g., contraceptives, etc.) and menstrual cycle controlling agents. Moreover, these are also useful in the livestock industry for the control fo the estrus of animals and also for the improvement in the quality of meat and for the control of the growth of animals, as well as in the marine products industry as spawning promoters for fishes. Thus, cyclo(Phg-D-Arg(Tos)-Phe-D-Ala-Trp) (Phg = L-phenylglycine, Tos = tosyl), prepd. by std. 9-fluorenylmethoxycarbonyl (Fmoc) chem. on a Wang resin, exhibited IC50 = 0.07 .mu.M in a LH-RH receptor assay. Ref. compd. cyclo(Tyr-D-Trp-Leu-Arg-Trp-Pro) showed IC50 = 10 .mu.M in the same assay.

L4 ANSWER 65 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1996:734039 CAPLUS

DN 126:60327

TI Synthesis of Modified Carboxyl Binding Pockets of Vancomycin and Teicoplanin

AU Bois-Choussy, Michele; Neuville, Luc; Beugelmans, Rene; Zhu, Jieping  
CS Institut de Chimie des Substances Naturelles, CNRS, Gif-sur-Yvette, 91198, Fr.

SO Journal of Organic Chemistry (1996), 61(26), 9309-9322

CODEN: JOCEAH; ISSN: 0022-3263

PB American Chemical Society

DT Journal

LA English

OS CASREACT 126:60327

IT **173775-55-8P 174759-45-6P**

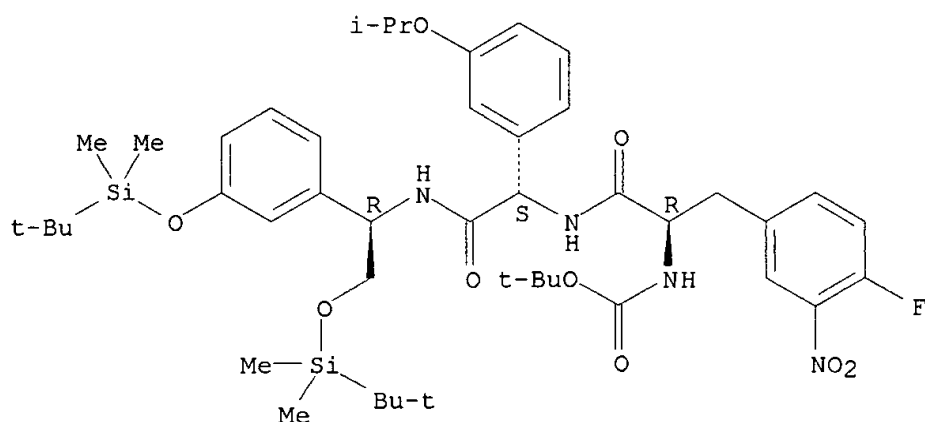
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of modified carboxyl binding pockets of vancomycin and teicoplanin)

RN 173775-55-8 CAPLUS

CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]-4-fluoro-3-nitro-D-phenylalanyl-N-[(1R)-2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-[3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]phenyl]ethyl]-2-[3-(1-methylethoxy)phenyl]-, (2S)- (9CI) (CA INDEX NAME)

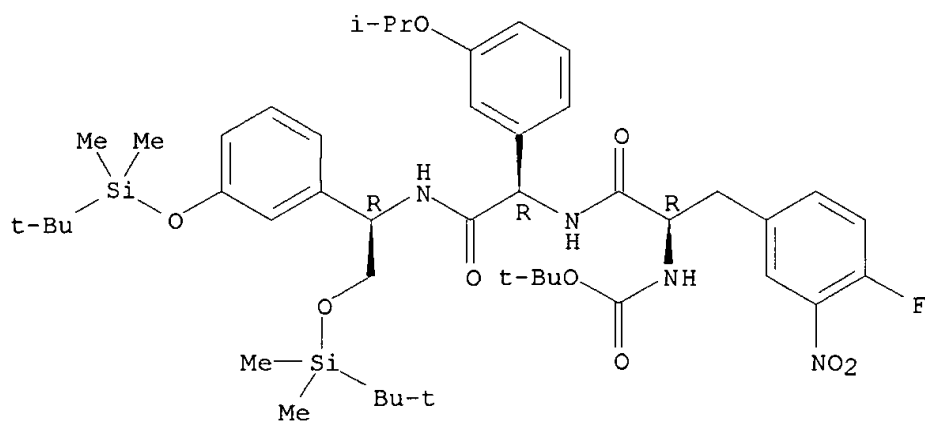
Absolute stereochemistry. Rotation (+).



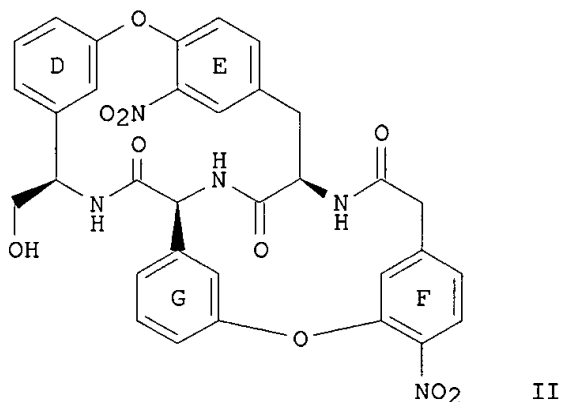
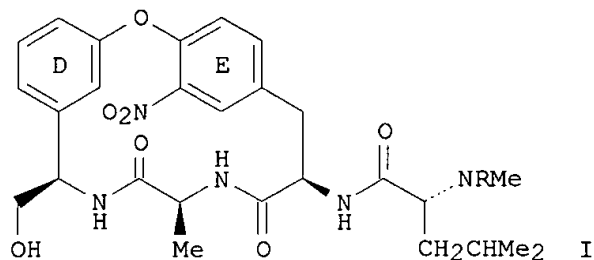
RN 174759-45-6 CAPLUS

CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]-4-fluoro-3-nitro-D-phenylalanyl-N-[(1R)-2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-[3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]phenyl]ethyl]-2-[3-(1-methylethoxy)phenyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



GI



AB Sixteen-membered macrocycle I (R = H) and 16+14 bicyclic compd. II, incorporating a terminal primary hydroxyl group in the peptide sequence, have been designed and synthesized. The syntheses feature the use of an efficient cycloetherification based on an intramol. SNAr reaction for the formation of biaryl ether bonds. Cyclization of a linear tetrapeptide, prep'd. via a convergent [2+2] segment coupling, gave macrocycle I (R = Boc) (P configuration) as a single isolable atropisomer. Removal of the Boc protecting group afforded the modified carboxyl binding pocket of vancomycin (I; R = H). A sequential 2-fold intramol. SNAr reaction has been used to construct the model bicyclic system (i.e. II) of the D-O-E-F-O-G ring of teicoplanin. Cyclization conditions (CsF, DMF, room temp.) are sufficiently mild that the configuration of the racemization-prone arylglycine residue was not affected. Chiral amino acid and amino alc. building blocks were prep'd. using Evans' asym. azidation method and Schollkopf's bislactim ether as a chiral glycine template. I showed interesting conformational properties compared to vancomycin and its binding with Ac-D-Ala was studied by NMR titrn. expts. A dissocn. const. ( $K_d = 5 \times 10^{-4}$ ) was calcd. by a curve fitting method. II is currently the most advanced synthetic intermediate toward the total synthesis of teicoplanin.

L4 ANSWER 66 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1996:380219 CAPLUS

DN 125:114281

TI Acyclic ethylenediamine derivatives

IN O'Neill, Brian T.

PA Pfizer Inc., USA

SO U.S., 16 pp., Cont.-in-part of U.S. Ser. No. 790,934, abandoned.

CODEN: USXXAM

DT Patent  
LA English  
FAN.CNT 2

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO.   | DATE     |
|----|--|------|----------|-------------------|----------|
| PI | US 5521220   | A    | 19960528 | US 1994-240657    | 19940720 |
|    |  |      |          | US 1991-790934 B2 | 19911112 |
|    |  |      |          | WO 1992-US7730 W  | 19920918 |
|    |  |      |          | WO 1992-US7730    | 19920918 |
|    | WO 9310073   | A1   | 19930527 |                   |          |
|    | W: AU, CA, FI, HU, JP, KR, NO, US                              |      |          |                   |          |
|    | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE |      |          |                   |          |
|    |  |      |          | US 1991-790934 A2 | 19911112 |
|    | CA 2324959   | C    | 20021112 | CA 1992-2324959   | 19920918 |
|    |  |      |          | US 1991-790934 A  | 19911112 |
|    |  |      |          | CA 1992-2123403A3 | 19920918 |

## PATENT FAMILY INFORMATION:

FAN 1993:670782

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO.   | DATE     |
|----|--|------|----------|-------------------|----------|
| PI | WO 9310073   | A1   | 19930527 | WO 1992-US7730    | 19920918 |
|    | W: AU, CA, FI, HU, JP, KR, NO, US                              |      |          |                   |          |
|    | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE |      |          |                   |          |
|    |  |      |          | US 1991-790934 A2 | 19911112 |
|    | AU 9226813   | A1   | 19930615 | AU 1992-26813     | 19920918 |
|    |  |      |          | US 1991-790934 A  | 19911112 |
|    |  |      |          | WO 1992-US7730 A  | 19920918 |
|    | EP 613458  | A1   | 19940907 | EP 1992-921029    | 19920918 |
|    | EP 613458  | B1   | 19980107 |                   |          |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE  |      |          |                   |          |
|    |  |      |          | US 1991-790934 A  | 19911112 |
|    |  |      |          | WO 1992-US7730 W  | 19920918 |
|    | JP 06510792  | T2   | 19941201 | JP 1992-509229    | 19920918 |
|    | JP 2614408   | B2   | 19970528 |                   |          |
|    |  |      |          | US 1991-790934 A  | 19911112 |
|    |  |      |          | WO 1992-US7730 W  | 19920918 |
|    | HU 70741   | A2   | 19951030 | HU 1994-1337      | 19920918 |
|    |  |      |          | US 1991-790934 A  | 19911112 |
|    | AT 161821  | E    | 19980115 | AT 1992-921029    | 19920918 |
|    |  |      |          | US 1991-790934 A  | 19911112 |
|    | ES 2111650   | T3   | 19980316 | ES 1992-921029    | 19920918 |
|    |  |      |          | US 1991-790934 A  | 19911112 |
|    | CA 2324959   | C    | 20021112 | CA 1992-2324959   | 19920918 |
|    |  |      |          | US 1991-790934 A  | 19911112 |
|    |  |      |          | CA 1992-2123403A3 | 19920918 |
|    | ZA 9208682   | A    | 19940511 | ZA 1992-8682      | 19921111 |
|    |  |      |          | US 1991-790934 A  | 19911112 |
|    | FI 9402187   | A    | 19940511 | FI 1994-2187      | 19940511 |
|    |  |      |          | US 1991-790934 A  | 19911112 |
|    |  |      |          | WO 1992-US7730 W  | 19920918 |
|    | NO 9401784   | A    | 19940511 | NO 1994-1784      | 19940511 |
|    |  |      |          | US 1991-790934 A  | 19911112 |
|    |  |      |          | WO 1992-US7730 A  | 19920918 |
|    | US 5521220   | A    | 19960528 | US 1994-240657    | 19940720 |
|    |  |      |          | US 1991-790934 B2 | 19911112 |
|    |  |      |          | WO 1992-US7730 W  | 19920918 |
|    | FI 2001000083  | A    | 20010115 | FI 2001-83        | 20010115 |
|    |  |      |          | US 1991-790934 A  | 19911112 |

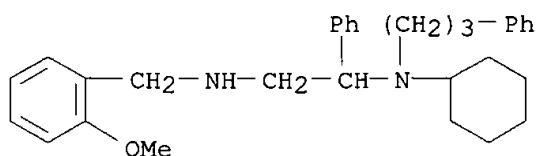
WO 1992-US7730 W 19920918

OS MARPAT 125:114281

IT **150917-46-7P**RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 150917-46-7 CAPLUS

CN 1,2-Ethanediamine, N1-cyclohexyl-N2-[(2-methoxyphenyl)methyl]-1-phenyl-N1-(3-phenylpropyl)- (9CI) (CA INDEX NAME)



AB PhCH(NHR<sub>1</sub>)CH<sub>2</sub>NHCH<sub>2</sub>R<sub>2</sub> (I; R<sub>1</sub> = alkyl, cycloalkyl; R<sub>2</sub> = aryl) and their salts were prepd. for treatment of inflammatory and central nervous system disorders. Thus, .alpha.-(cyclohexylamino)benzeneacetonitrile, which was prepd. from BzH, cyclohexylamine, and KCN, was reduced with diisobutylaluminum hydride to give N-cyclohexyl-1-phenyl-1,2-ethanediamine, which reacted with o-anisaldehyde and Na triacetoxyborohydride to give I (R<sub>1</sub> = cyclohexyl, R<sub>2</sub> = 2-methoxyphenyl). The dihydrochloride of this product was also described.

L4 ANSWER 67 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1996:379679 CAPLUS

DN 125:59130

TI Preparation of ethers of aspartate protease substrate isosteres as antivirals.

IN Bold, Guido; Capraro, Hans-Georg; Faessler, Alexander; Lang, Marc; Bhagwat, Shripad Subray; Khanna, Satish Chandra; Lazdins, Janis Karlis; Mestan, Juergen

PA Ciba-Geigy A.-G., Switz.

SO Eur. Pat. Appl., 131 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|----|---|------|----------|-----------------|------------|
| PI | EP 708085   | A2   | 19960424 | EP 1995-115938  | 19951010   |
|    | EP 708085   | A3   | 19971008 |                 |            |
|    | EP 708085   | B1   | 20020717 |                 |            |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE |      |          |                 |            |
|    |   |      |          | CH 1994-3140    | A 19941019 |
|    |   |      |          | CH 1995-2382    | A 19950821 |
|    | AT 220661   | E    | 20020815 | AT 1995-115938  | 19951010   |
|    |   |      |          | CH 1994-3140    | A 19941019 |
|    |   |      |          | CH 1995-2382    | A 19950821 |
|    | ES 2180600  | T3   | 20030216 | ES 1995-115938  | 19951010   |
|    |   |      |          | CH 1994-3140    | A 19941019 |
|    |   |      |          | CH 1995-2382    | A 19950821 |
|    | AU 9534279  | A1   | 19960502 | AU 1995-34279   | 19951012   |
|    | AU 707283   | B2   | 19990708 |                 |            |
|    |   |      |          | CH 1994-3140    | A 19941019 |



|             |    |          |                  |            |
|-------------|----|----------|------------------|------------|
| FI 9504913  | A  | 19960420 | CH 1995-2382     | A 19950821 |
|             |    |          | FI 1995-4913     | 19951016   |
|             |    |          | CH 1994-3140     | A 19941019 |
| CA 2160763  | AA | 19960420 | CH 1995-2382     | A 19950821 |
|             |    |          | CA 1995-2160763  | 19951017   |
|             |    |          | CH 1994-3140     | A 19941019 |
| BG 63042    | B1 | 20010228 | CH 1995-2382     | A 19950821 |
|             |    |          | BG 1995-100067   | 19951017   |
|             |    |          | CH 1994-3140     | A 19941019 |
| SK 282339   | B6 | 20020107 | CH 1995-2382     | A 19950821 |
|             |    |          | SK 1995-1285     | 19951017   |
|             |    |          | CH 1994-3140     | A 19941019 |
| CZ 290123   | B6 | 20020612 | CH 1995-2382     | A 19950821 |
|             |    |          | CZ 1995-2713     | 19951017   |
|             |    |          | CH 1994-3140     | A 19941019 |
| ZA 9508782  | A  | 19960419 | CH 1995-2382     | A 19950821 |
|             |    |          | ZA 1995-8782     | 19951018   |
| NO 9504142  | A  | 19960422 | CH 1994-3140     | A 19941019 |
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|             |    |          | CH 1994-3140     | A 19941019 |
| CN 1132756  | A  | 19961009 | CH 1995-2382     | A 19950821 |
|             |    |          | CN 1995-120506   | 19951018   |
|             |    |          | CH 1994-3140     | A 19941019 |
| HU 74744    | A2 | 19970228 | CH 1995-2382     | A 19950821 |
|             |    |          | HU 1995-3007     | 19951018   |
|             |    |          | CH 1994-3140     | A 19941019 |
| RU 2164229  | C2 | 20010320 | CH 1995-2382     | A 19950821 |
|             |    |          | RU 1995-118112   | 19951018   |
|             |    |          | CH 1994-3140     | A 19941019 |
| JP 08208580 | A2 | 19960813 | CH 1995-2382     | A 19950821 |
| JP 3192070  | B2 | 20010723 | JP 1995-295024   | 19951019   |
|             |    |          | CH 1994-3140     | A 19941019 |
|             |    |          | CH 1995-2382     | A 19950821 |
| BR 9504466  | A  | 19970520 | BR 1995-4466     | 19951019   |
|             |    |          | CH 1994-3140     | A 19941019 |
|             |    |          | CH 1995-2382     | A 19950821 |
| US 5663200  | A  | 19970902 | US 1995-545170   | 19951019   |
|             |    |          | CH 1994-3140     | A 19941019 |
|             |    |          | CH 1995-2382     | A 19950821 |
| PL 184292   | B1 | 20020930 | PL 1995-311027   | 19951019   |
|             |    |          | CH 1994-3140     | A 19941019 |
|             |    |          | CH 1995-2382     | A 19950821 |
| TW 397813   | B  | 20000711 | TW 1995-84111501 | 19951101   |
|             |    |          | CH 1994-3140     | A 19941019 |
| US 5807891  | A  | 19980915 | US 1997-838347   | 19970408   |
|             |    |          | CH 1994-3140     | A 19941019 |
|             |    |          | CH 1995-2382     | A 19950821 |
| US 5935976  | A  | 19990810 | US 1995-545170   | A319951019 |
|             |    |          | US 1998-138076   | 19980821   |
|             |    |          | CH 1994-3140     | A 19941019 |
|             |    |          | CH 1995-2382     | A 19950821 |
|             |    |          | US 1995-545170   | A319951019 |
|             |    |          | US 1997-838347   | A319970408 |

OS MARPAT 125:59130

IT **178048-10-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

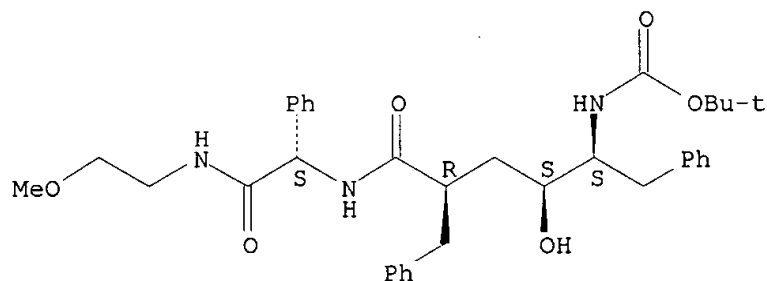
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of ethers of aspartate protease substrate isosteres as antivirals)

RN 178048-10-7 CAPLUS

CN 2-Oxa-5,8,14-triazapentadecan-15-oic acid, 12-hydroxy-6,9-dioxo-7-phenyl-10,13-bis(phenylmethyl)-, 1,1-dimethylethyl ester, [7S-(7R\*,10S\*,12R\*,13R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 178049-01-9P

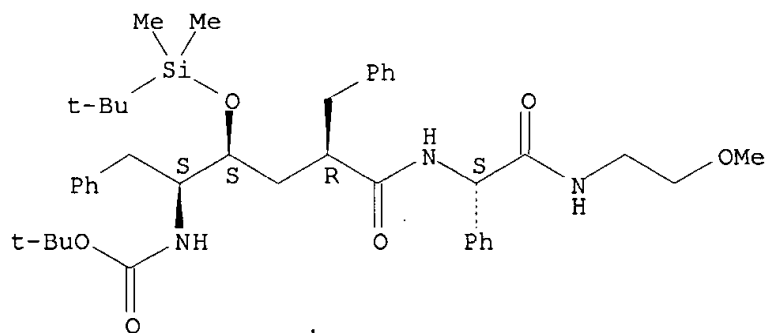
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of ethers of aspartate protease substrate isosteres as antivirals)

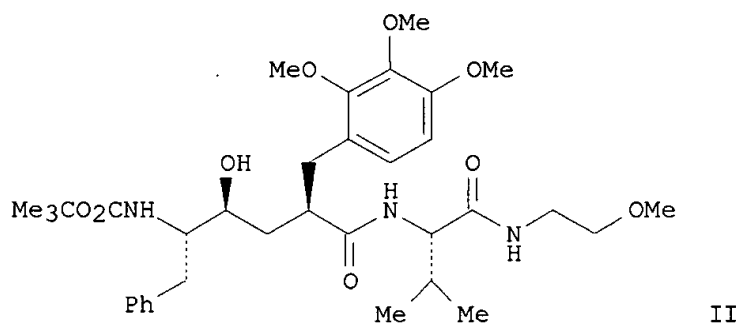
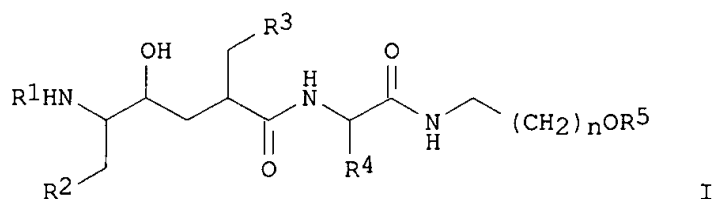
RN 178049-01-9 CAPLUS

CN 2-Oxa-5,8,14-triazapentadecan-15-oic acid, 12-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6,9-dioxo-7-phenyl-10,13-bis(phenylmethyl)-, 1,1-dimethylethyl ester, [7S-(7R\*,10S\*,12R\*,13R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB Title compds. [I; R1 = (substituted) alkoxyalkanoyl, alkoxy carbonyl, alkanoyl, arylcarbonyl, heterocyclylcarbonyl, phenylalkanoyl, arylsulfonyl, amino acid residue; R2, R3 = (substituted) cyclohexyl, cyclohexenyl, Ph, naphthyl, tetrahydronaphthyl; R4 = alkyl, cyclohexyl, Ph; R5 = alkyl; n = 1, 2; provided .gtoreq.1 salt forming group is present], were prepd. Thus, title compd. (II), prepd. via 5(S)-[1(S)-(tert-butoxycarbonylamino)-2-phenylethyl]-3(R)-[(2,3,4-trimethoxyphenyl)methyl]dihydrofuran-2(3H)-one, at 12.5 nM combined with 12.5 nM indavir gave 76.6% inhibition of reverse transcriptase in a coculture of CEM-SS and H9/HIV-1/IIIB. Capsule formulations contg. II are given.

L4 ANSWER 68 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1996:285987 CAPLUS

DN 124:333315

TI Study on the activation mechanism of neurokinin receptors

AU Abe, Junko; Fujinaka, Hidetake; Mukai, Hidehito; Munekata, Eisuke

CS Institute Applied Biochemistry, University Tsukuba, Tsukuba, 305, Japan

SO Peptide Chemistry (1996), Volume Date 1995, 33rd, 277-80

CODEN: PECHDP; ISSN: 0388-3698

PB Protein Research Foundation

DT Journal

LA English

IT **176840-46-3**

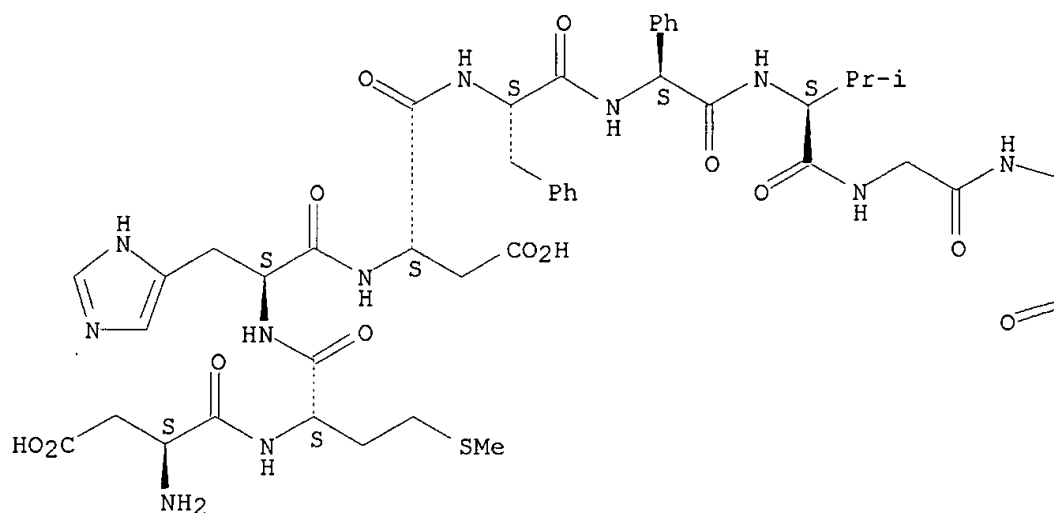
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (activation mechanism of neurokinin receptors)

RN 176840-46-3 CAPLUS

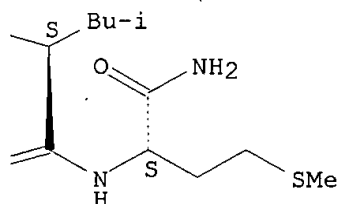
CN Neurokinin B (swine spinal cord), 6-(L-2-phenylglycine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



AB The peptide analogs of substance P (SP), neurokinin A (NKA) and neurokinin B (NKB) in which Phe residue at the 5th position from carboxyl-terminus are replaced by phenylglycine (Phg) and homophenylalanine (Hph) were prepd. and the pharmacol. significances of the arom. amino acid at this position were comparatively investigated.

L4 ANSWER 69 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1996:271993 CAPLUS

DN 125:59116

TI Synthetic studies towards glycopeptide antibiotics: synthesis of the 16-membered cyclic tripeptide (DOEG ring) system of teicoplanin

AU Rao, A. V. Rama; Reddy, K. Laxma; Rao, A. Srinivasa; Vittal, T. V. S. K.; Reddy, M. M.; Pathi, P. L.

CS Indian Inst. Chem. Technol., Hyderabad, 500 007, India

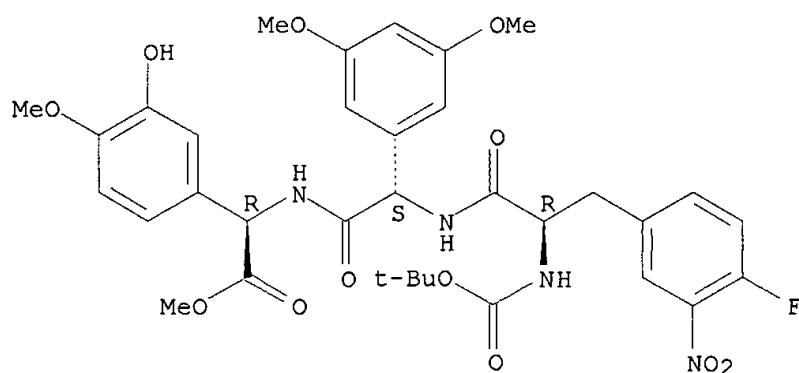
SO Tetrahedron Letters (1996), 37(17), 3023-6

CODEN: TELEAY; ISSN: 0040-4039

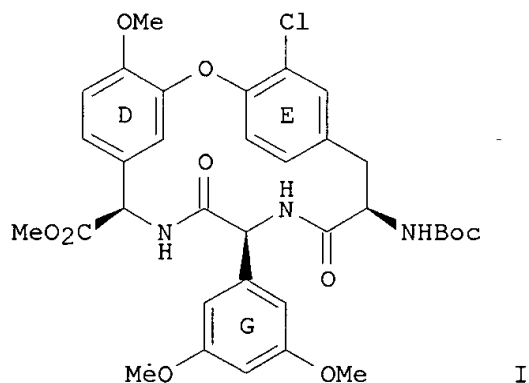
PB Elsevier

DT Journal  
 LA English  
 IT **178217-07-7P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (prepn. of the 16-membered cyclic tripeptide system of teicoplanin)  
 RN 178217-07-7 CAPLUS  
 CN Glycine, N-[L-2-(3,5-dimethoxyphenyl)-N-[N-[(1,1-dimethylethoxy)carbonyl]-  
 4-fluoro-3-nitro-D-phenylalanyl]glycyl]-D-2-(3-hydroxy-4-methoxyphenyl)-,  
 methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB The synthesis of the 16-membered cyclic DOEG ring system I of teicoplanin, which forms the binding pocket for the carboxylate region of terminal D-Ala-D-Ala of the bacterial cell wall, via macroetherification of a linear tripeptide is described.

L4 ANSWER 70 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1996:241976 CAPLUS  
 DN 124:331828

TI Inhibitors of Human Immunodeficiency Virus Type 1 Protease Containing  
2-Aminobenzyl-Substituted 4-Amino-3-hydroxy-5-phenylpentanoic acid:  
Synthesis, Activity, and Oral Bioavailability

AU Lehr, Philipp; Billich, Andreas; Charpiot, Brigitte; Ettmayer, Peter;  
Scholz, Dieter; Rosenwirth, Brigitte; Gstach, Hubert

CS Sandoz Research Institute, Vienna, A-1235, Austria

SO Journal of Medicinal Chemistry (1996), 39(10), 2060-7  
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

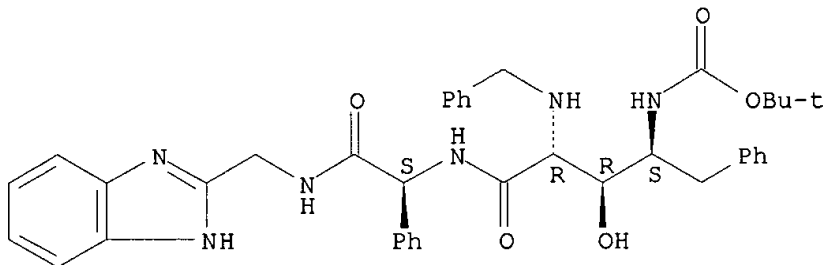
LA English

IT **176388-97-9P**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. and bioavailability and HIV-1 protease inhibitory activity of  
(aminobenzyl)hydroxyphenylpentanoates)

RN 176388-97-9 CAPLUS

CN L-Lyxonamide, N-[2-[(1H-benzimidazol-2-ylmethyl)amino]-2-oxo-1-  
phenylethyl]-2,4,5-trideoxy-4-[[[(1,1-dimethylethoxy)carbonyl]amino]-5-  
phenyl-2-[(phenylmethyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Systematic modifications of HIV protease inhibitor (2R,3S,4S)-4-  
[[[(benzyloxycarbonyl)-L-valyl]amino]-3-hydroxy-2-[(4-methoxybenzyl)amino]-  
5-(phenylpentanoyl)-L-valine 2-(aminomethyl)benzimidazole amide led to a  
novel series of inhibitors with a shortened, modified carboxy terminus.  
Their synthesis, in vitro enzyme inhibitory data, and antiviral activities  
are reported. Of particular interest are derivs. featuring the  
(1S,2R)-1-amino-2-hydroxyindan moiety at the P2'-position since some of  
them exhibit substantial oral bioavailability in mice. The influence of  
aq. soly. and structural parameters on the oral resorption of the  
inhibitors is discussed. Optimum enhancement of oral bioavailability was  
obsd. with L-tert-leucine in P2-position, resulting in the discovery of  
(2R,3S,4S)-4-[[[(benzyloxycarbonyl)-L-tert-leucyl]amino]-3-hydroxy-2-[(4-  
methoxybenzyl)amino]-5-phenylpentanoic acid (1S,2R)-1-amino-2-hydroxyindan  
amide which combines high antiviral activity (IC<sub>50</sub> = 250 nM) with a good  
pharmacokinetic profile (AUC = 82.5 .mu.M.cntdot.h at a dose of 125 mg/kg  
po in mice).

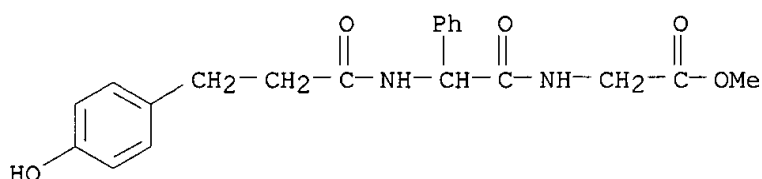
L4 ANSWER 71 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1996:211368 CAPLUS

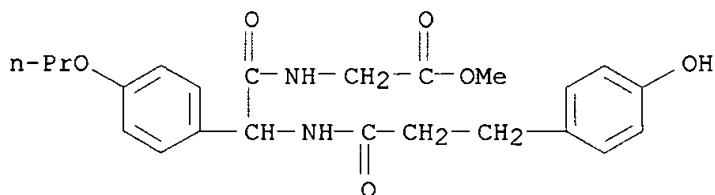
DN 124:344085

TI Solid-phase, parallel syntheses by Ugi multicomponent condensation

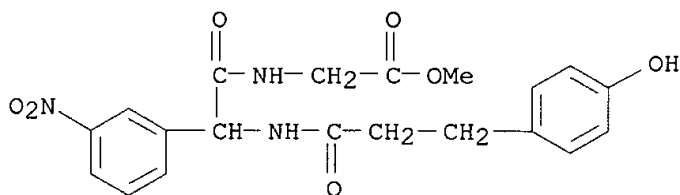
AU Tempest, Paul A.; Brown, S. David; Armstrong, Robert W.  
 CS Dep. Chem. Biochem., Univ. California, Los Angeles, CA, 90095-1569, USA  
 SO Angewandte Chemie, International Edition in English (1996), 35(6), 640-2  
 CODEN: ACIEAY; ISSN: 0570-0833  
 PB VCH  
 DT Journal  
 LA English  
 IT **176845-79-7P 176845-81-1P 176845-82-2P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of amino acid amides and dipeptides by Ugi multicomponent  
 condensations on a solid support)  
 RN 176845-79-7 CAPLUS  
 CN Glycine, N-[N-[3-(4-hydroxyphenyl)-1-oxopropyl]-2-phenylglycyl]-, methyl  
 ester (9CI) (CA INDEX NAME)



RN 176845-81-1 CAPLUS  
 CN Glycine, N-[N-[3-(4-hydroxyphenyl)-1-oxopropyl]-2-(4-propoxyphenyl)glycyl]-,  
 methyl ester (9CI) (CA INDEX NAME)



RN 176845-82-2 CAPLUS  
 CN Glycine, N-[N-[3-(4-hydroxyphenyl)-1-oxopropyl]-2-(3-nitrophenyl)glycyl]-,  
 methyl ester (9CI) (CA INDEX NAME)



AB Ugi multicomponent condensation is used to prep. a 96-member library of  
 amino acid amides and dipeptides, e.g. R2CONHCHR1CO-Gly-OMe (R1 = Et, Ph,  
 cyclohexylmethyl, etc., R2 = H, cyclopropyl, Ph2CH, etc.), on a solid  
 support.

L4 ANSWER 72 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1996:209976 CAPLUS

DN 124:242373

TI Treatment of diseases caused by sebaceous gland disorders with acyl coA cholesterol acyl transferase inhibitors

IN Mayne, James T.

PA Pfizer Inc., USA

SO Eur. Pat. Appl., 12 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

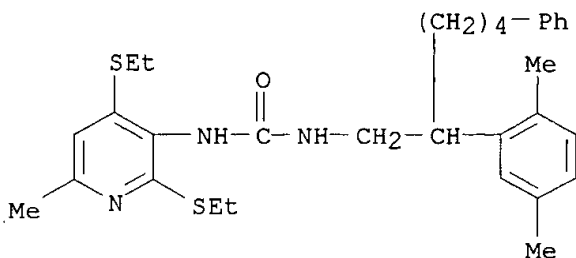
|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.   | DATE     |
|----|---|------|----------|-------------------|----------|
| PI | EP 699439   | A2   | 19960306 | EP 1995-305594    | 19950810 |
|    | EP 699439   | A3   | 19960626 |                   |          |
|    | EP 699439   | B1   | 19991006 |                   |          |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE |      |          |                   |          |
|    | US 6133326  | A    | 20001017 | US 1994-298735 A  | 19940831 |
|    | AT 185271   | E    | 19991015 | US 1994-298735    | 19940831 |
|    |   |      |          | AT 1995-305594    | 19950810 |
|    | ES 2136252  | T3   | 19991116 | US 1994-298735 A  | 19940831 |
|    |   |      |          | ES 1995-305594    | 19950810 |
|    | CA 2157142  | AA   | 19960301 | US 1994-298735 A  | 19940831 |
|    | CA 2157142  | C    | 19980609 | CA 1995-2157142   | 19950829 |
|    |   |      |          | US 1994-298735 A  | 19940831 |
|    | JP 08099903   | A2   | 19960416 | JP 1995-242297    | 19950829 |
|    | JP 3266473  | B2   | 20020318 |                   |          |
|    |   |      |          | US 1994-298735 A  | 19940831 |
|    | JP 2002053494   | A2   | 20020219 | JP 2001-241766    | 19950829 |
|    |   |      |          | US 1994-298735 A  | 19940831 |
|    |   |      |          | JP 1995-242297 A3 | 19950829 |
|    | US 6271268  | B1   | 20010807 | US 2000-536480    | 20000327 |
|    |   |      |          | US 1994-298735 A1 | 19940831 |

IT 157548-92-0

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (treatment of sebaceous gland disorders with cholesterol acyl transferase inhibitors)

RN 157548-92-0 CAPLUS

CN Urea, N-[2,4-bis(ethylthio)-6-methyl-3-pyridinyl]-N'-[2-(2,5-dimethylphenyl)-6-phenylhexyl]- (9CI) (CA INDEX NAME)



AB A method of treating diseases caused by sebaceous gland disorders, e.g. acne, comprises administering a compn. contg. an acyl coA cholesterol acyl



transferase (ACAT) inhibitor or prodrug therefor. S-N-[2,4-bis(methylthio)-6-methylpyrid-3-yl]-(2-hexylthio)decanamide (I) was formulated into topical preps. Oral administration of I to beagle dogs at a dose of 50 mg/kg/day for 14 days resulted in almost complete atrophy of the acinar components of the eyelid sebaceous glands with dilation of the central collecting duct.

L4 ANSWER 73 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1995:998406 CAPLUS

DN 124:203098

TI Preparation of peptide factor Xa inhibitors as antithrombotics.

IN Al-Obeidi, Fahad; Lebl, Michal; Ostrem, James A.; Safar, Pavel; Stierandova, Alena; Strop, Peter; Walser, Armin

PA Selectide Corp., USA

SO PCT Int. Appl., 107 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.  | DATE     |
|----|---|------|----------|------------------|----------|
| PI | WO 9529189  | A1   | 19951102 | WO 1995-US5268   | 19950425 |
|    | W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN |      |          |                  |          |
|    | RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG                |      |          |                  |          |
|    | CA 2186497  | AA   | 19951102 | US 1994-233054 A | 19940426 |
|    |   |      |          | CA 1995-2186497  | 19950425 |
|    |   |      |          | US 1994-233054 A | 19940426 |
|    | AU 9523683  | A1   | 19951116 | AU 1995-23683    | 19950425 |
|    | AU 707653   | B2   | 19990715 |                  |          |
|    |   |      |          | US 1994-233054 A | 19940426 |
|    |   |      |          | WO 1995-US5268 W | 19950425 |
|    | ZA 9503361  | A    | 19960112 | ZA 1995-3361     | 19950425 |
|    |   |      |          | US 1994-233054 A | 19940426 |
|    | EP 758341   | A1   | 19970219 | EP 1995-917736   | 19950425 |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE   |      |          |                  |          |
|    |   |      |          | US 1994-233054 A | 19940426 |
|    |   |      |          | WO 1995-US5268 W | 19950425 |
|    | CN 1147261  | A    | 19970409 | CN 1995-192811   | 19950425 |
|    |   |      |          | US 1994-233054 A | 19940426 |
|    | HU 76346  | A2   | 19970828 | HU 1996-2954     | 19950425 |
|    |   |      |          | US 1994-233054 A | 19940426 |
|    | JP 10503477   | T2   | 19980331 | JP 1995-527853   | 19950425 |
|    |   |      |          | US 1994-233054 A | 19940426 |
|    |   |      |          | WO 1995-US5268 W | 19950425 |
|    | RU 2152954  | C1   | 20000720 | RU 1996-122647   | 19950425 |
|    |   |      |          | US 1994-233054 A | 19940426 |
|    |   |      |          | WO 1995-US5268 W | 19950425 |
|    | EE 3973   | B1   | 20030217 | EE 1996-146      | 19950425 |
|    |   |      |          | US 1994-233054 A | 19940426 |
|    |   |      |          | WO 1995-US5268 W | 19950425 |
|    | IL 113505   | A1   | 19991231 | IL 1995-113505   | 19950426 |
|    |   |      |          | US 1994-233054 A | 19940426 |
|    | TW 409129   | B    | 20001021 | TW 1995-84104681 | 19950511 |

|            |   |          |                           |
|------------|---|----------|---------------------------|
| FI 9604317 | A | 19961025 | US 1994-233054 A 19940426 |
|            |   |          | FI 1996-4317 19961025     |
|            |   |          | US 1994-233054 A 19940426 |
| NO 9604553 | A | 19961227 | WO 1995-US5268 W 19950425 |
|            |   |          | NO 1996-4553 19961025     |
|            |   |          | US 1994-233054 A 19940426 |
| LT 4218    | B | 19970925 | WO 1995-US5268 W 19950425 |
|            |   |          | LT 1996-151 19961025      |
| LV 11740   | B | 19971220 | US 1994-233054 A 19940426 |
|            |   |          | LV 1996-410 19961115      |
| US 5849510 | A | 19981215 | US 1994-233054 A 19940426 |
|            |   |          | US 1997-947794 19971008   |
|            |   |          | US 1994-233054 B219940426 |
|            |   |          | US 1995-428404 B119950425 |

OS MARPAT 124:203098

IT **174132-22-0P**

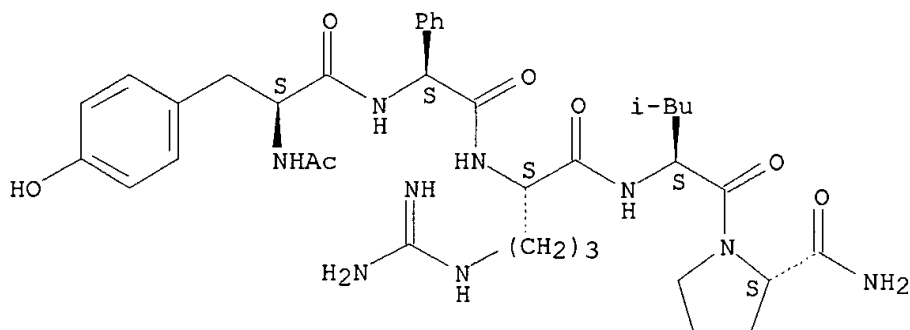
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of peptide factor Xa inhibitors as antithrombotics)

RN 174132-22-0 CAPLUS

CN L-Prolinamide, N-acetyl-L-tyrosyl-L-2-phenylglycyl-L-arginyl-L-leucyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB A1-A2-(A3)<sub>m</sub>-B [m = 0, 1; A1 = R1-R2-R3; A2 = R4-R5-R6; A3 = R7-R8-R9; R1 = (substituted) 1-20 amino acid residues, R11CO, R11R12X; X = N, CH, NCO; R11, R12 = H, alkyl, acyl, aryl, aralkyl, protecting group; R2 = CR99R100; R99, R100 = H, (substituted) alkyl, aralkyl, heteroaralkyl, heteroaryl; R3 = CO, CH2, CHR99CO, etc.; R4 = CH2, imino; R5 = CR201R202; R201, R202 = H, (substituted) alkyl, aryl, aralkyl; R6 = CO, CH2, CHR99CO; R7 = (substituted) R4; R8 = CR210R211; R210, R211 = H, (substituted) alkyl, alkylaryl, heterocyclyl; R9 = CO, CH2, CHR99CO; B = (substituted) 1-20 amino acid residues, amino, OH, alkoxy, acyloxy, etc.; with provisos], were prepd. Thus, Ac-Tyr-Chg-Arg-NH<sub>2</sub> (Chg = cyclohexylglycyl) inhibited coagulation in human plasma with EC<sub>50</sub> = 2.5 .mu.M.

L4 ANSWER 74 OF 148 CAPLUS COPYRIGHT 2003 ACS

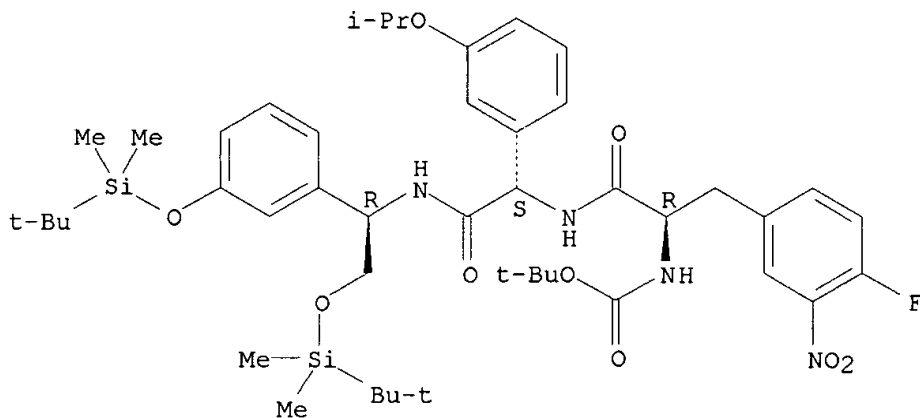
AN 1995:968838 CAPLUS

DN 124:176884

TI The first synthesis of a model bicyclic D-O-E-F-O-G ring of teicoplanin via sequential intramolecular SNAr reactions

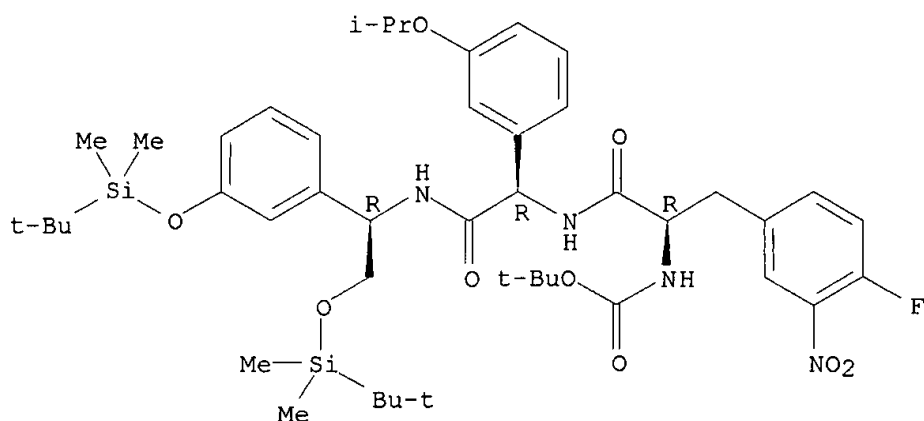
AU Beugelmans, Rene; Neuville, Luc; Bois-Choussy, Michele; Zhu, Jieping  
 CS Inst. Chimie Substances Naturelles, Gif-sur-Yvette, 91198, Fr.  
 SO Tetrahedron Letters (1995), 36(48), 8787-90  
 CODEN: TELEAY; ISSN: 0040-4039  
 PB Elsevier  
 DT Journal  
 LA English  
 OS CASREACT 124:176884  
 IT **173775-55-8P 174759-45-6P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (synthesis of model bicyclic ring of teicoplanin via sequential  
 intramol. reactions)  
 RN 173775-55-8 CAPLUS  
 CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]-4-fluoro-3-nitro-D-  
 phenylalanyl-N-[(1R)-2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-[3-[[[(1,1-  
 dimethylethyl)dimethylsilyl]oxy]phenyl]ethyl]-2-[3-(1-methylethoxy)phenyl]-  
 , (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

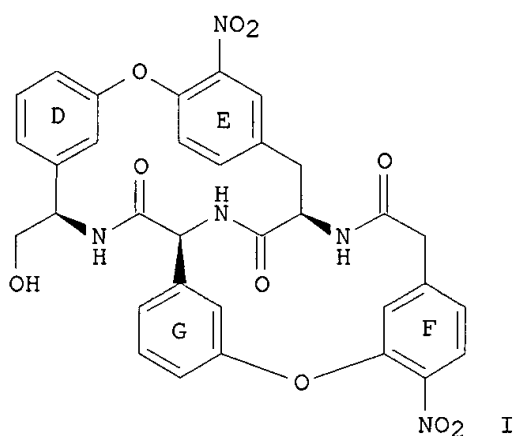


RN 174759-45-6 CAPLUS  
 CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]-4-fluoro-3-nitro-D-  
 phenylalanyl-N-[(1R)-2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-[3-[[[(1,1-  
 dimethylethyl)dimethylsilyl]oxy]phenyl]ethyl]-2-[3-(1-methylethoxy)phenyl]-  
 , (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



GI



AB A model bicyclic D-O-E-F-O-G ring (I) of teicoplanin has been efficiently synthesized via sequential intramol. SNAr reactions.

L4 ANSWER 75 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1995:938729 CAPLUS

DN 124:105558

TI 3D-Quantitative Structure-Activity Relationships of Human Immunodeficiency Virus Type-1 Proteinase Inhibitors: Comparative Molecular Field Analysis of 2-Heterosubstituted Statine Derivatives-Implications for the Design of Novel Inhibitors

AU Kroemer, Romano T.; Ettmayer, Peter; Hecht, Peter

CS SANDOZ Forschungsinstitut Ges. m. b. H, Vienna, A-1235, Austria

SO Journal of Medicinal Chemistry (1995), 38(25), 4917-28

CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

IT 172215-84-8, SDZ 283559

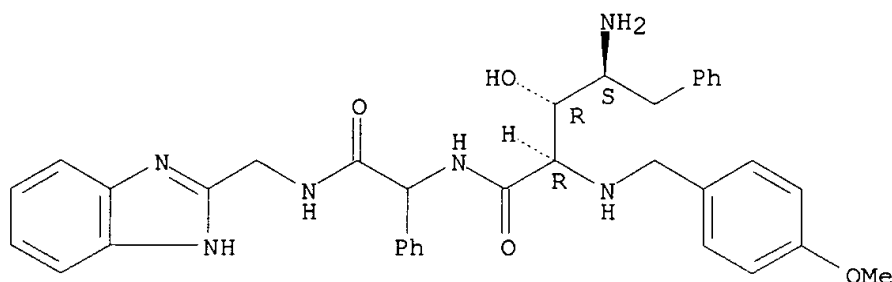
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(3D-quant. structure-activity relationships of human immunodeficiency virus type-1 proteinase inhibitors using comparative mol. field anal. of 2-heterosubstituted statine derivs.)

RN 172215-84-8 CAPLUS

CN L-Lyxonamide, 4-amino-N-[2-[(1H-benzimidazol-2-ylmethyl)amino]-2-oxo-1-phenylethyl]-2,4,5-trideoxy-2-[[[(4-methoxyphenyl)methyl]amino]-5-phenyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB A set of 100 novel 2-heterosubstituted statine derivs. inhibiting human immunodeficiency virus type-1 proteinase has been investigated by comparative mol. field anal. To combine the structural information available from x-ray analyses with a predictive quant. structure-activity relation (QSAR) model, docking expts. of a prototype compd. into the receptor were performed, and the 'active conformation' was detd. The structure of the receptor was taken from the published x-ray anal. of the proteinase with bound MVT-101, the latter compd. exhibiting high structural similarity with the inhibitors investigated. The validity of the resulting QSARs was confirmed in four different ways. (1) The common parameters, namely, the cross-validated  $r^2$  values obtained by the leave-one-out (LOO) method ( $r^2_{ev} = 0.572-0.593$ ), and (2) the accurate prediction of a test set of 67 compds. ( $q^2 = 0.552-0.569$ ) indicated a high consistency of the models. (3) Repeated analyses with two randomly selected cross-validation groups were performed and the cross-validated  $r^2$  values monitored. The resulting av.  $r^2$  values were of similar magnitudes compared to those obtained by the LOO method. (4) The coeff. fields were compared with the steric and electrostatic properties of the receptor and showed a high level of compatibility. Further anal. of the results led to the design of a novel class of highly active compds. contg. an addnl. linkage between P1' and P3'. The predicted activities of these inhibitors were also in good agreement with the exptl. detd. values.

L4 ANSWER 76 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1995:835557 CAPLUS

DN 123:256542

TI Preparation of annelated dihydropyridines

IN Roos, Otto; Loesel, Walter; Arndts, Dietrich

PA Boehringer Ingelheim KG, Germany

SO Ger. Offen., 28 pp.

CODEN: GWXXBX

DT Patent  
 LA German  
 FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.   | DATE     |
|----|---|------|----------|-------------------|----------|
| PI | DE 4343683  | A1   | 19950622 | DE 1993-4343683   | 19931221 |
|    | CA 2178209  | AA   | 19950629 | CA 1994-2178209   | 19941214 |
|    | WO 9517389  | A1   | 19950629 | DE 1993-4343683A  | 19931221 |
|    |   |      |          | WO 1994-EP4150    | 19941214 |
|    | W: AU, CA, CN, JP, KR, PL, RU   |      |          |                   |          |
|    | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE    |      |          | DE 1993-4343683A  | 19931221 |
|    | AU 9512433  | A1   | 19950710 | AU 1995-12433     | 19941214 |
|    | AU 699208   | B2   | 19981126 |                   |          |
|    |   |      |          | DE 1993-4343683A  | 19931221 |
|    |   |      |          | WO 1994-EP4150 W  | 19941214 |
|    | EP 736011   | A1   | 19961009 | EP 1995-903342    | 19941214 |
|    | EP 736011   | B1   | 20000726 |                   |          |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE |      |          | DE 1993-4343683A  | 19931221 |
|    |   |      |          | WO 1994-EP4150 W  | 19941214 |
|    | CN 1138325  | A    | 19961218 | CN 1994-194572    | 19941214 |
|    | CN 1044905  | B    | 19990901 |                   |          |
|    |   |      |          | DE 1993-4343683A  | 19931221 |
|    | JP 09506882   | T2   | 19970708 | JP 1994-517154    | 19941214 |
|    |   |      |          | DE 1993-4343683A  | 19931221 |
|    |   |      |          | WO 1994-EP4150 W  | 19941214 |
|    | RU 2136664  | C1   | 19990910 | RU 1996-115153    | 19941214 |
|    |   |      |          | DE 1993-4343683A  | 19931221 |
|    |   |      |          | WO 1994-EP4150 W  | 19941214 |
|    | AT 194978   | E    | 20000815 | AT 1995-903342    | 19941214 |
|    |   |      |          | DE 1993-4343683A  | 19931221 |
|    |   |      |          | WO 1994-EP4150 W  | 19941214 |
|    | ES 2149958  | T3   | 20001116 | ES 1995-903342    | 19941214 |
|    |   |      |          | DE 1993-4343683A  | 19931221 |
|    | ZA 9410115  | A    | 19950621 | ZA 1994-10115     | 19941220 |
|    |   |      |          | DE 1993-4343683A  | 19931221 |
|    | US 5661157  | A    | 19970826 | US 1994-360867    | 19941221 |
|    |   |      |          | DE 1993-4343683A  | 19931221 |
|    | TW 404941   | B    | 20000911 | TW 1994-83112295  | 19941228 |
|    |   |      |          | DE 1993-4343683A  | 19931221 |
|    | US 5968948  | A    | 19991019 | US 1997-857643    | 19970516 |
|    |   |      |          | DE 1993-4343683A  | 19931221 |
|    |   |      |          | US 1994-360867 A3 | 19941221 |
|    | US 6136819  | A    | 20001024 | US 1999-329443    | 19990610 |
|    |   |      |          | DE 1993-4343683A  | 19931221 |
|    |   |      |          | US 1994-360867 A3 | 19941221 |
|    |   |      |          | US 1997-857643 A3 | 19970516 |

OS MARPAT 123:256542

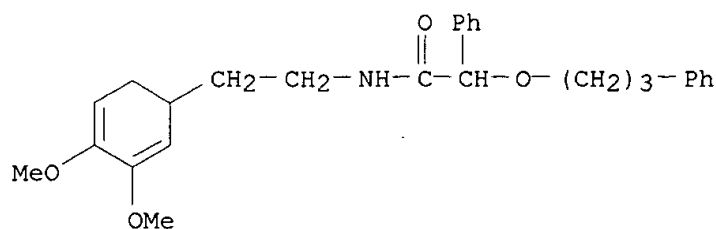
IT **168545-16-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of annelated dihydropyridines from)

RN 168545-16-2 CAPLUS

CN Benzeneacetamide, N-[2-(3,4-dimethoxy-2,4-cyclohexadien-1-yl)ethyl]-.alpha.-(3-phenylpropoxy)- (9CI) (CA INDEX NAME)



GI For diagram(s), see printed CA Issue.

AB The title compds. [I; A = benzo, thieno, indolo; B = O, S, (un)substituted CH<sub>2</sub>; R<sub>2</sub> = OH, alkoxy, benzyloxy, halogen, alkyl, methanesulfonyloxy, etc.; R<sub>3</sub> = 2- or 3-thienyl, (un)substituted Ph, alkyl, cycloalkylalkyl; R<sub>4</sub> = (un)branched alkenyl or alkynyl, alkoxy, dialkylamino, heterocyclyl, Ph, etc.; m = 0-3] (e.g., II), useful as calcium-channel blockers (no data), are prepd. by the intramol. cyclocondensation of arom. amides (III) (e.g., IV) in the presence of condensing agents (e.g., POCl<sub>3</sub>), and I-contg. formulations are also presented.

L4 ANSWER 77 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1995:701735 CAPLUS

DN 123:112727

TI Preparation of dipeptide derivatives of 5-amino-4-hydroxyhexanoic acid as HIV protease inhibitors.

IN Bold, Guido; Lang, Marc; Faessler, Alexander; Capraro, Hans-Georg; Bhagwat, Shripad

PA Ciba-Geigy A.-G., Switz.

SO Eur. Pat. Appl., 116 pp.

CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 618222   | A2   | 19941005 | EP 1994-810133  | 19940302 |
|    | EP 618222   | A3   | 19970102 |                 |          |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE |      |          |                 |          |
|    | AU 9457588  | A1   | 19940915 | CH 1993-772     | 19930311 |
|    | AU 678202   | B2   | 19970522 | AU 1994-57588   | 19940304 |
|    |   |      |          | CH 1993-772     | 19930311 |
|    | FI 9401064  | A    | 19940912 | FI 1994-1064    | 19940307 |
|    |   |      |          | CH 1993-772     | 19930311 |
|    | CA 2118661  | AA   | 19940912 | CA 1994-2118661 | 19940309 |
|    |   |      |          | CH 1993-772     | 19930311 |
|    | NO 9400853  | A    | 19940912 | NO 1994-853     | 19940310 |
|    |   |      |          | CH 1993-772     | 19930311 |
|    | ZA 9401668  | A    | 19940913 | ZA 1994-1668    | 19940310 |
|    |   |      |          | CH 1993-772     | 19930311 |
|    | HU 67089  | A2   | 19950130 | HU 1994-720     | 19940310 |
|    |   |      |          | CH 1993-772     | 19930311 |
|    | CN 1112125  | A    | 19951122 | CN 1994-104099  | 19940310 |
|    |   |      |          | CH 1993-772     | 19930311 |
|    | JP 07316191   | A2   | 19951205 | JP 1994-67908   | 19940311 |
|    |   |      |          | CH 1993-772     | 19930311 |

OS MARPAT 123:112727

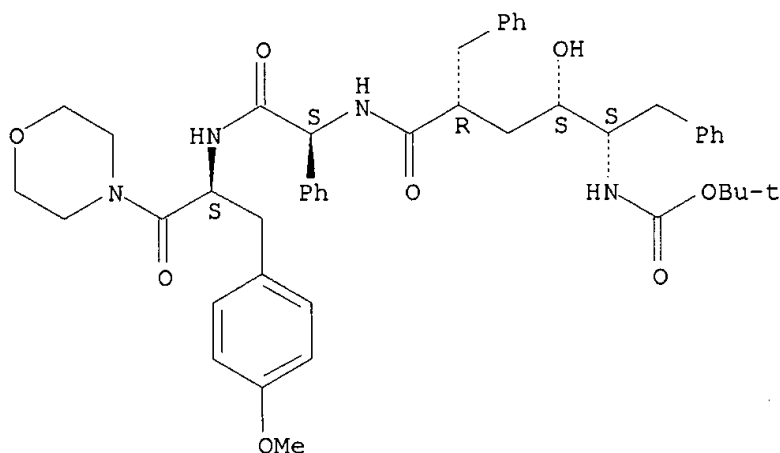
IT **165453-83-8P 165453-86-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. of dipeptide derivs. of 5-amino-4-hydroxyhexanoic acid as HIV protease inhibitors)

RN 165453-83-8 CAPLUS

CN Carbamic acid, [2-hydroxy-5-[[2-[[1-[(4-methoxyphenyl)methyl]-2-(4-morpholinyl)-2-oxoethyl]amino]-2-oxo-1-phenylethyl]amino]-5-oxo-1,4-bis(phenylmethyl)pentyl]-, 1,1-dimethylethyl ester, [1S-[1R\*,2R\*,4S\*,5[R\*(R\*)]]]- (9CI) (CA INDEX NAME)

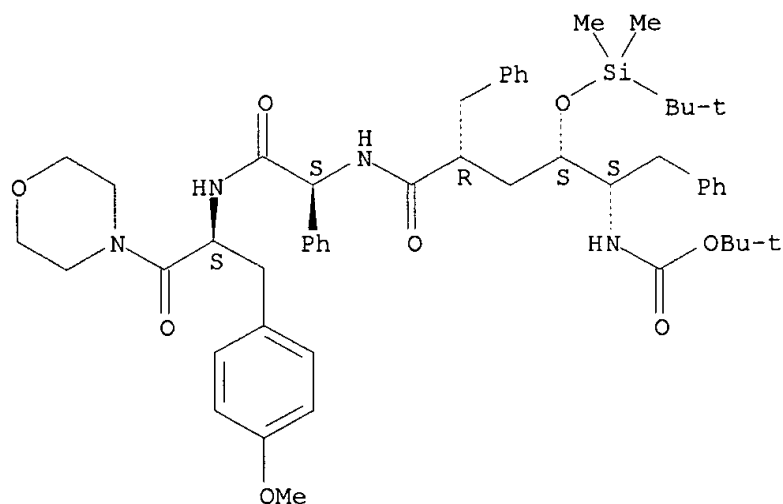
Absolute stereochemistry.



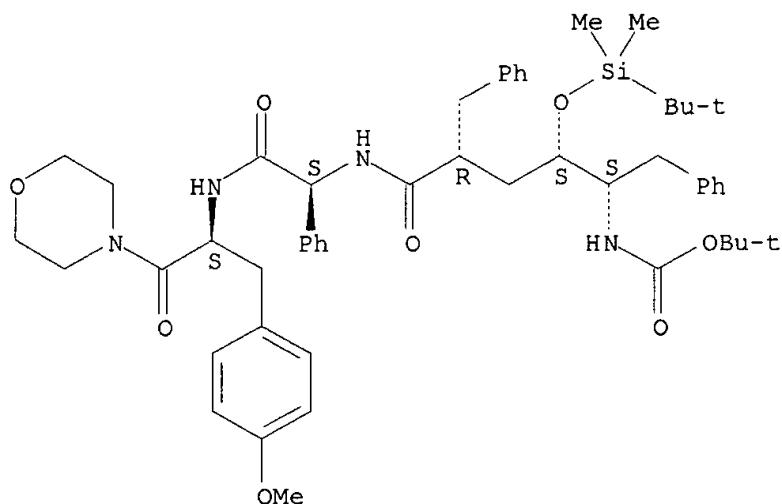
RN 165453-86-1 CAPLUS

CN Carbamic acid, [2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-[[2-[[1-[(4-methoxyphenyl)methyl]-2-(4-morpholinyl)-2-oxoethyl]amino]-2-oxo-1-phenylethyl]amino]-5-oxo-1,4-bis(phenylmethyl)pentyl]-, 1,1-dimethylethyl ester, [1S-[1R\*,2R\*,4S\*,5[R\*(R\*)]]]- (9CI) (CA INDEX NAME)

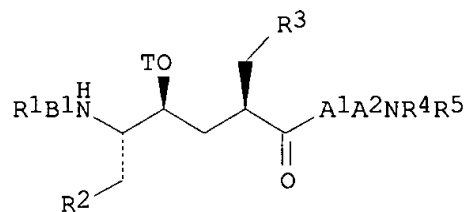
Absolute stereochemistry.



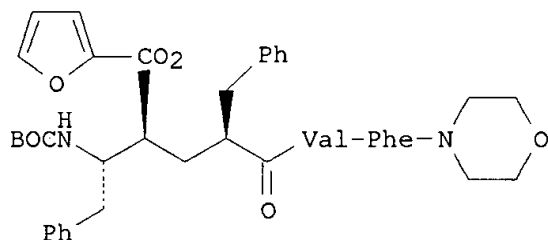




GI



I



II

AB Title compds. [I; T = R<sub>6</sub>CO; R<sub>6</sub> = (substituted) hydrocarbyl in which .gtoreq.1 C atom is replaced by a heteroatom; R<sub>1</sub> = H, alkoxycarbonyl, heterocyclylcarbonyl, (substituted) benzyloxycarbonyl, heterocyclyloxycarbonyl, etc.; A<sub>1</sub>, B<sub>1</sub> = bond, amino acid residue; R<sub>2</sub>, R<sub>3</sub> = (substituted) Ph, cyclohexyl; A<sub>2</sub> = amino acid residue; A<sub>1</sub>A<sub>2</sub> = dipeptide residue whose central amide bond is reduced; NR<sub>4</sub>R<sub>5</sub> = (substituted) morpholino, thiomorpholino], were prepd. Title compd. II was prepd. by soln. phase coupling reactions. I inhibited HIV-1 protease with IC<sub>50</sub> = 10<sup>-7</sup>-10<sup>-9</sup> M.

L4 ANSWER 78 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1995:679270 CAPLUS

DN 123:75087

TI Structure-activity relationships of dermorphin analogs containing

N-substituted amino acids in the 2-position of the peptide sequence

AU Schmidt, Ralf; Kalman, Andras; Chung, Nga N.; Lemieux, Carole; Horvath, Csaba; Schiller, Peter W.

CS Lab. Chem. Biol. Peptide Res., Clin. Res. Inst. Montreal, Quebec, Can.

SO International Journal of Peptide & Protein Research (1995), 46(1), 47-55  
CODEN: IJPPC3; ISSN: 0367-8377

PB Munksgaard

DT Journal

LA English

IT **165128-29-0**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

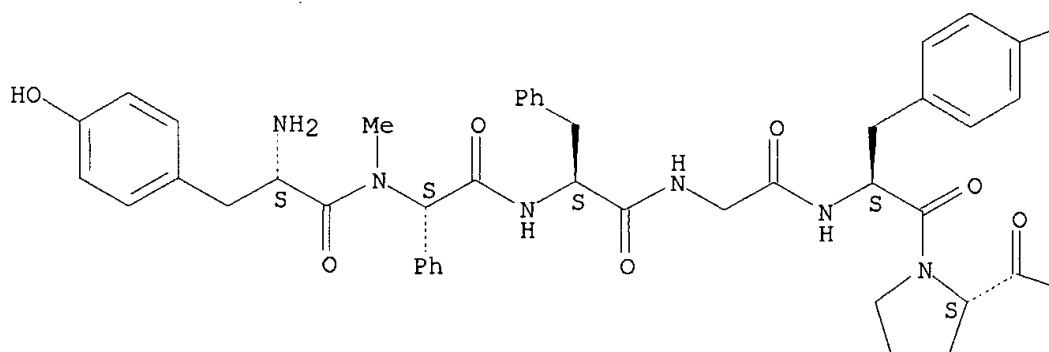
(structure-activity relationships of dermorphin analogs contg.  
N-substituted amino acids in the 2-position of the peptide sequence)

RN 165128-29-0 CAPLUS

CN Dermorphin, 2-(N-methyl-L-2-phenylglycine)- (9CI) (CA INDEX NAME)

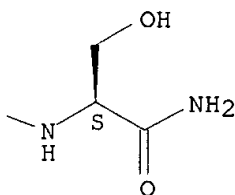
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

—OH

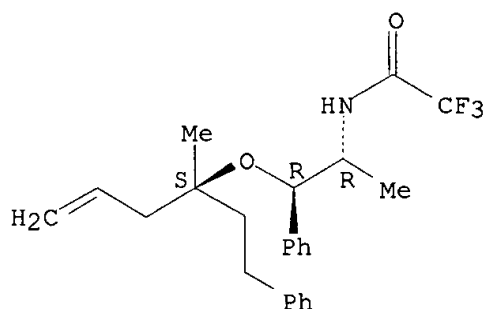


AB A series of dermorphin analogs contg. an N-alkylated amino acid residue Xaa in the 2-position of the peptide sequence was synthesized (Xaa =

N-methylalanine, proline, pipecolic acid, N-methylphenylalanine, 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid [Tic]). These peptides have the potential of assuming a cis Tyr1-Xaa2 peptide bond. Their in vitro opioid activity profiles were detd. in .mu.- and .delta.-receptor-representative binding assays and bioassays. Aside from [D-Pro2]dermorphin, all analogs showed high affinity for .mu.- and/or .delta.-opioid receptors. Whereas most compds. were full .mu.-agonists in the guinea pig ileum (GPI) assay, [Tic2]dermorphin (compd. 7) was a partial .mu.-agonist. Replacement of Gly4 in 7 with Phe resulted in an analog (8) with weak .mu.-antagonist activity. Furthermore, analogs 7 and 8 both were potent .delta.-antagonists (Kc = 3-40 nM) against the .delta.-agonists Leu-enkephalin, DPDPE and deltorphin I in the mouse vas deferens (MVD) assay. Compd. 3, contg. L-Pro in the 2-position, turned out to be one of the most .mu.-receptor-selective linear dermorphin analogs reported to date. Low-temp. HPLC expts. using micropellicular octadecyl silica as stationary phase revealed conformational heterogeneity of the dermorphin analogs which was ascribed to cis-trans isomerization around the Tyr1-Xaa2- and Tyr5-Pro6 peptide bonds. In the case of analog 7 four sep. peaks corresponding to the four possible isomers were apparent at -5.degree.. Since opioid peptide analogs with a non-N-alkylated L-amino acid residue in the 2-position are nearly inactive and cannot assume a cis peptide bond at the 1-2 position, these results support the hypothesis that the bioactive conformation of opioid peptides contg. an N-alkylated L-amino acid residue in position 2 is characterized by a cis Tyr1-Xaa2 peptide bond.

L4 ANSWER 79 OF 148 CAPLUS COPYRIGHT 2003 ACS  
AN 1995:568922 CAPLUS  
DN 123:111518  
TI Enantioselective Synthesis of Tertiary Homoallylic Alcohols via  
Diastereoselective Addition of Allylsilanes to Ketones  
AU Tietze, Lutz F.; Schiemann, Kai; Wegner, Christoph  
CS Institute of Organic Chemistry, Georg-August-Universitaet, Goettingen,  
D-37077, Germany  
SO Journal of the American Chemical Society (1995), 117(21), 5851-2  
CODEN: JACSAT; ISSN: 0002-7863  
PB American Chemical Society  
DT Journal  
LA English  
OS CASREACT 123:111518  
IT **165823-95-0P 166021-67-6P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(enantioselective synthesis of tertiary homoallylic alcs. via  
diastereoselective addn. of allylsilanes to ketones)  
RN 165823-95-0 CAPLUS  
CN Acetamide, 2,2,2-trifluoro-N-[(1R,2R)-1-methyl-2-[[ (1S)-1-methyl-1-(2-phenylethyl)-3-butenyl]oxy]-2-phenylethyl]- (9CI) (CA INDEX NAME)

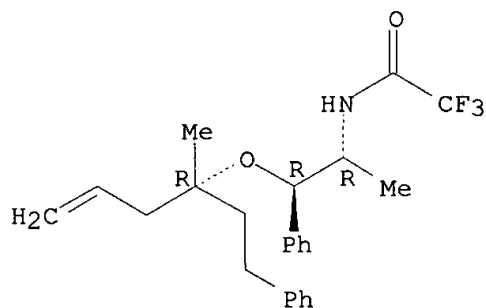
Absolute stereochemistry. Rotation (+).



RN 166021-67-6 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[1-methyl-2-[[1-methyl-1-(2-phenylethyl)-3-butenyl]oxy]-2-phenylethyl]-, [1R-[1R\*,2R\*(R\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Enantiopure tertiary homoallylic alcs.  $\text{CH}_2\text{:CHCH}_2\text{CRMeOH}$  ( $\text{R} = \text{alkyl}$ ) can be obtained from the corresponding homoallylic ethers  $\text{CH}_2\text{:CHCH}_2\text{CRMeOR1}$  [4,  $\text{R1} = \text{residue of (1R,2R)-N-(trifluoroacetyl)norpseudoephedrine}$ ] by treatment with sodium in liq. ammonia. The ethers 4 are formed highly selectively by treatment of the ketones  $\text{MeCOR}$  with the trimethylsilyl ether of N-trifluoroacetylnorpseudoephedrine in the presence of catalytic amts. of  $\text{Me}_3\text{SiB(OTf)}_4$  or  $\text{Me}_3\text{SiOTf/TfOH}$  ( $\text{Tf} = \text{CF}_3\text{SO}_2$ ) followed by addn. of allyltrimethylsilane. The yield was about 90% (based on conversion) and the diastereoselectivity was about 90:10. Using iso-Pr Me ketone a selectivity of >95:5 was obtained; thus only one diastereomer could be detected.

L4 ANSWER 80 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1995:480169 CAPLUS

DN 122:240447

TI Preparation of peptideamide analogs as tachykinin antagonists.

IN Pieper, Helmut; Austel, Volkhard; Jung, Birgit; Buerger, Erich; Entzeroth, Michael

PA Karl Thomas GmbH, Germany

SO Ger. Offen., 101 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

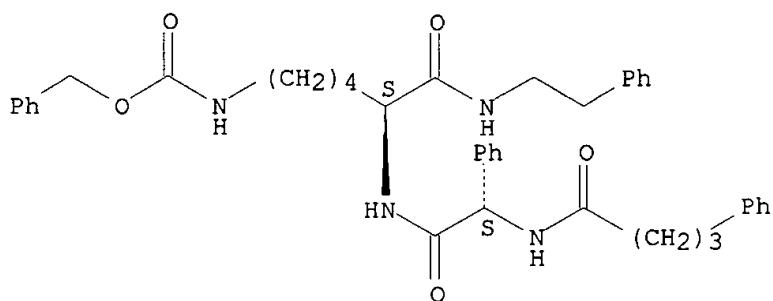
PATENT NO.

KIND DATE

APPLICATION NO. DATE

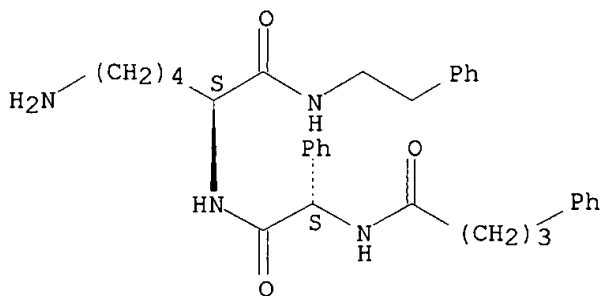
PI DE 4243858 A1 19940630 DE 1992-4243858 19921223  
 DE 1992-4243858 19921223  
 OS MARPAT 122:240447  
 IT **162177-25-5P 162177-26-6P 162177-27-7P**  
**162177-28-8P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of, as tachykinin antagonist)  
 RN 162177-25-5 CAPLUS  
 CN L-Lysinamide, N-(1-oxo-4-phenylbutyl)-L-2-phenylglycyl-N-(2-phenylethyl)-N6-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 162177-26-6 CAPLUS  
 CN L-Lysinamide, N-(1-oxo-4-phenylbutyl)-L-2-phenylglycyl-N-(2-phenylethyl)-, monohydrobromide (9CI) (CA INDEX NAME)

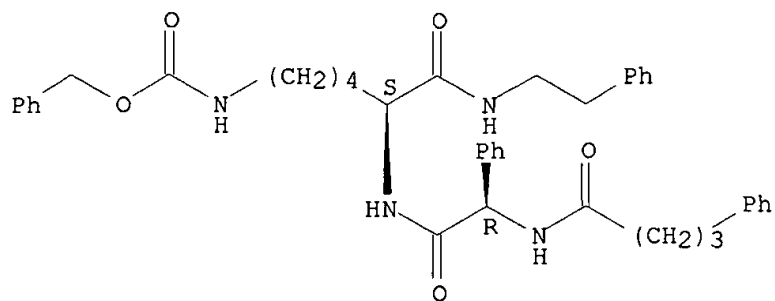
Absolute stereochemistry.



● HBr

RN 162177-27-7 CAPLUS  
 CN L-Lysinamide, N-(1-oxo-4-phenylbutyl)-D-2-phenylglycyl-N-(2-phenylethyl)-N6-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

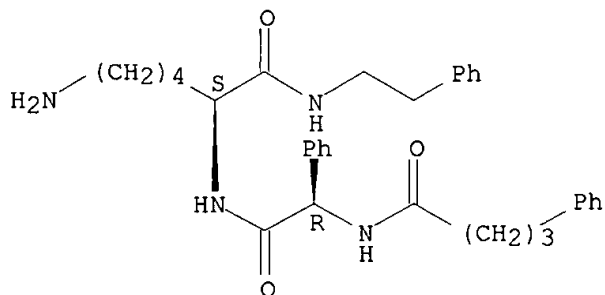
Absolute stereochemistry.



RN 162177-28-8 CAPLUS

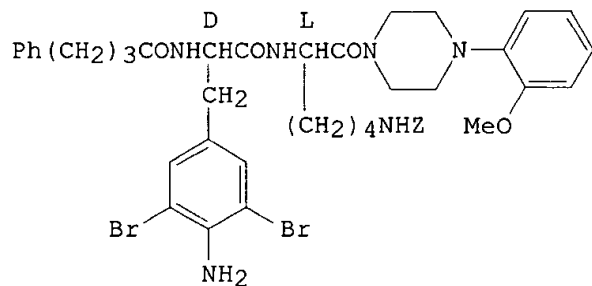
CN L-Lysinamide, N-(1-oxo-4-phenylbutyl)-D-2-phenylglycyl-N-(2-phenylethyl)-, monohydrobromide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HBr

GI



I

AB R4R5NACONHCHR3CXNR1R2 [A = 1,2-cyclopentylene, CHR6; R6 = H, (substituted) alkyl, Ph; R1 = H, (Ph- or pyridyl-substituted) alkyl; R2 = H, (amino- or

guanidino-substituted) Ph, pyridyl, (cyclohexyl-, Ph-, or pyridyl-substituted) alkyl, etc.; R1R2N = (substituted) piperazinyl; R3 = H, (phenyl)alkyl, guanidino- or amino-substituted alkyl, aminocarbonylalkyl, etc.; R4 = H, (phenyl)alkyl; R5 = protecting group, (substituted) alkyl, alkanoyl, alkoxy carbonyl, alkylaminocarbonyl, PhCO, naphthylcarbonyl, biphenylcarbonyl, PhSO<sub>2</sub>, etc.; X = (H, H), O, S; the C atom bearing the R3 substituent is L; the C atom bearing the R6 substituent is D or L], were prepd. Thus, title compd. I (prepd. by soln. phase methods) showed IC<sub>50</sub> = 2 nM for neurokinin-1 receptor binding with IM-9 cells. Tablets were prepd. contg. I.

L4 ANSWER 81 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1995:409660 CAPLUS

DN 123:9907

TI Prerequisite for His4 in deltorphin A for high .delta. opioid receptor selectivity

AU Salvadori, S.; Guerrini, R.; Forlani, V.; Bryant, S. D.; Attila, M.; Lazarus, L. H.

CS Dept. Pharm. Sci., Univ. Ferrara, Ferrara, Italy

SO Amino Acids (1994), 7(3), 291-304

CODEN: AACIE6; ISSN: 0939-4451

PB Springer

DT Journal

LA English

IT **163679-50-3P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

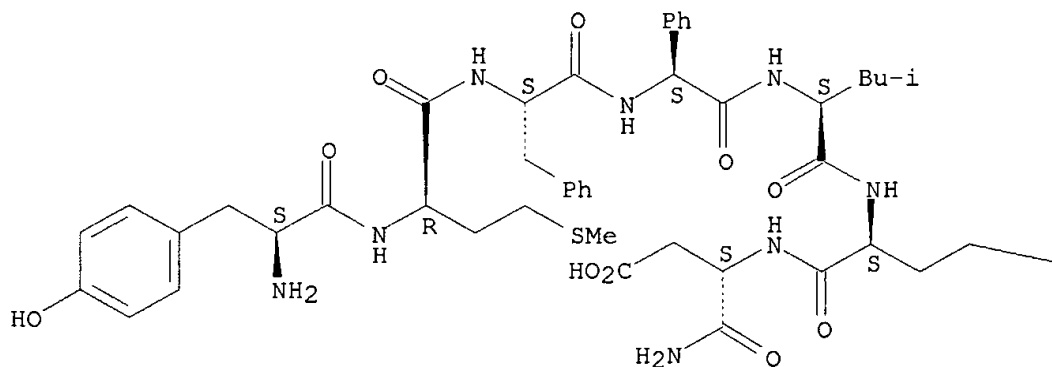
(.delta. opioid receptor selectivity of deltorphin A position 4 analogs)

RN 163679-50-3 CAPLUS

CN Deltorphin A, 4-(L-2-phenylglycine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



— SMe

AB Anal. of deltorphin A position 4 analogs included: backbone constrained MeHis, spinacine (Spi), MePhe, and tetrahydroisoquinoline-3-carboxylic acid (Tic); spatially confined side-chain phenylglycine (Phg); and imidazole alkylation of L- and D-His4 enantiomers. High  $\delta$  selectivity was lost with the following replacements; MeHis4, MePhe4 and Phg4 reduced  $\delta$  binding and the constrained residues also increased  $\mu$  binding; ring closure between the side-chain and amino group to yield Spi4 or Tic4 increased  $\mu$  affinity. Imidazole methylation of His4 marginally affected opioid binding and doubled  $\delta$  selectivity; alkylated D-His4 derivs. generally maintained  $\delta$  selectivity in spite of decreased  $\delta$  binding and by repulsion at the  $\mu$  receptor. Several low energy conformers of deltorphin A indicated that the His4 imidazole preferred a spatial orientation parallel to the phenolic side-chain of Tyr1 suggestive that this conformation might contribute to high  $\delta$  affinity and selectivity.

L4 ANSWER 82 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1994:557528 CAPLUS

DN 121:157528

TI Preparation of N-aryl- and N-heteroarylureas as inhibitors of cholesterol acyltransferase

IN Hamanaka, Ernest S.

PA Pfizer Inc., USA

SO PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO.   | DATE     |
|----|--|------|----------|-------------------|----------|
| PI | WO 9324458   | A1   | 19931209 | WO 1993-US3539    | 19930420 |
|    | W: AU, BG, BR, CA, CZ, DE, JP, KR, NO, NZ, RO, RU, SK, UA, US  |      |          |                   |          |
|    | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG |      |          |                   |          |
|    |  |      |          | US 1992-890050 A2 | 19920528 |
| AU | 9340283  | A1   | 19931230 | AU 1993-40283     | 19930420 |
|    |  |      |          | US 1992-890050 A  | 19920528 |
|    |  |      |          | WO 1993-US3539 A  | 19930420 |
| EP | 642498   | A1   | 19950315 | EP 1993-909519    | 19930420 |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE  |      |          |                   |          |
|    |  |      |          | US 1992-890050 A  | 19920528 |
|    |  |      |          | WO 1993-US3539 W  | 19930420 |
| JP | 07503737   | T2   | 19950420 | JP 1994-500522    | 19930420 |
|    |  |      |          | US 1992-890050 A  | 19920528 |



|            |    |          |                           |
|------------|----|----------|---------------------------|
| CA 2134359 | C  | 19970701 | WO 1993-US3539 W 19930420 |
| BR 9306421 | A  | 19980915 | CA 1993-2134359 19930420  |
|            |    |          | US 1992-890050 A 19920528 |
| HU 64303   | A2 | 19931228 | BR 1993-6421 19930420     |
| CN 1080919 | A  | 19940119 | US 1992-890050 A 19920528 |
| NO 9404530 | A  | 19941125 | WO 1993-US3539 W 19930420 |
| US 6001860 | A  | 19991214 | HU 1993-1552 19930527     |
|            |    |          | US 1992-890050 A 19920528 |
|            |    |          | CN 1993-106774 19930527   |
|            |    |          | US 1992-890050 A 19920528 |
|            |    |          | NO 1994-4530 19941125     |
|            |    |          | US 1992-890050 A 19920528 |
|            |    |          | WO 1993-US3539 A 19930420 |
|            |    |          | US 1995-343557 19950117   |
|            |    |          | US 1992-890050 B219920528 |
|            |    |          | WO 1993-US3539 W 19930420 |

## PATENT FAMILY INFORMATION:

FAN 1999:794333

|    | PATENT NO. | KIND | DATE     | APPLICATION NO.   | DATE     |
|----|------------|------|----------|---|----------|
| PI | US 6001860 | A    | 19991214 | US 1995-343557  | 19950117 |
|    |            |      |          | US 1992-890050 B219920528                                       |          |
|    |            |      |          | WO 1993-US3539 W 19930420                                       |          |
|    | WO 9324458 | A1   | 19931209 | WO 1993-US3539  | 19930420 |
|    | W:         |      |          | AU, BG, BR, CA, CZ, DE, JP, KR, NO, NZ, RO, RU, SK, UA, US      |          |
|    | RW:        |      |          | AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, |          |
|    |            |      |          | BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG          |          |
|    |            |      |          | US 1992-890050 A219920528                                       |          |

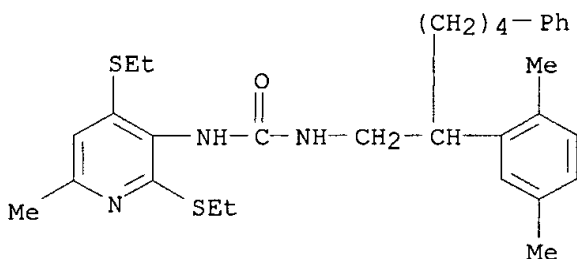
OS MARPAT 121:157528

IT **157548-92-0P**

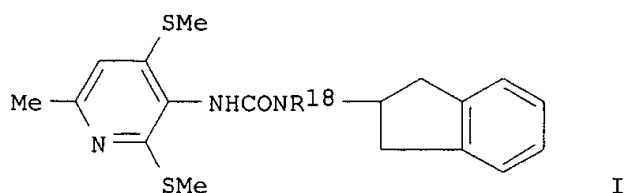
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of, as cholesterol acyltransferase inhibitor)

RN 157548-92-0 CAPLUS

CN Urea, N-[2,4-bis(ethylthio)-6-methyl-3-pyridinyl]-N'-[2-(2,5-dimethylphenyl)-6-phenylhexyl]- (9CI) (CA INDEX NAME)



GI



AB R1NHC(:X)NR17R18 [R1 = (hetero)aryl; R17 = (CH2)n(CR19R20)z(CH2)rR; R = aryl, heterocyclyl, etc.; R18 = H, (cyclo)alkyl, aralkyl, etc.; R19,R20 = H, (halo)alkyl, aralkyl, etc.; R19R20 = atoms to form a ring; X = O or S; n = 0-13; r = 0-4; z = 0 or 1] were prepd. as inhibitors of cholesterol acyltransferase (no data). Thus, 2-(4-isopropylbenzylamino)indane was condensed with 2,4-bis(methylthio)-6-methylpyridin-3-yl isocyanate to give title compd. I [R18 = 4-(Me2HC)C6H4CH2].

L4 ANSWER 83 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1994:271122 CAPLUS

DN 120:271122

TI Inhibition of matrix metalloproteinases by N-carboxyalkyl peptides

AU Chapman, Kevin T.; Kopka, Ihor E.; Durette, Philippe L.; Esser, Craig K.; Lanza, Thomas J.; Izquierdo-Martin, Maria; Niedzwiecki, Lisa; Chang, Benedict; Harrison, Richard K.; et al.

CS Dep. Med. Chem. Res., Merck Res. Lab., Rahway, NJ, 07065-0900, USA

SO Journal of Medicinal Chemistry (1993), 36(26), 4293-301

CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

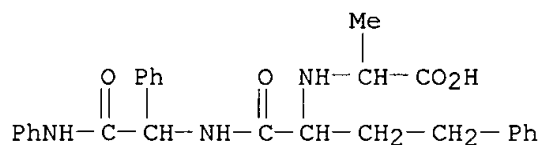
IT **147472-95-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)

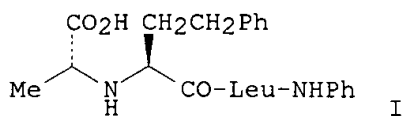
(prepn. and inhibition by, of stromelysin, collagenase, and gelatinase A)

RN 147472-95-5 CAPLUS

CN Glycinamide, N-(1-carboxyethyl)-4-phenyl-L-2-aminobutanoyl-L-N,2-diphenyl-, (R)- (9CI) (CA INDEX NAME)



GI

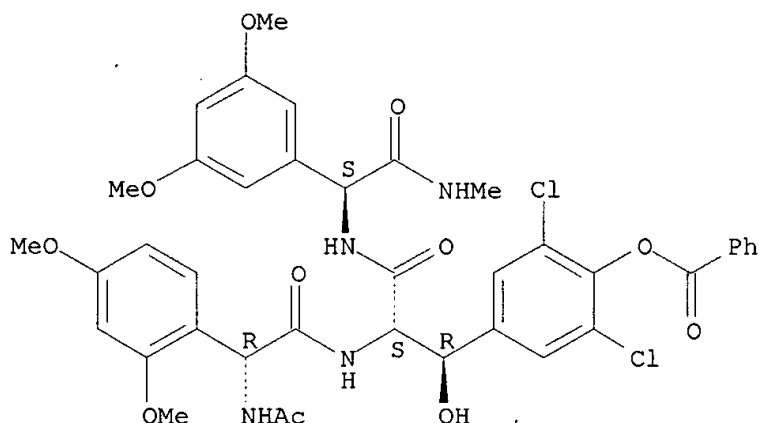


AB An extensive study of the requirements for effective binding of

N-carboxyalkyl peptides to human stromelysin, collagenase, and to a lesser extent, gelatinase A has been investigated. These efforts afforded inhibitors generally in the 100-400 nM range for these matrix metalloproteinases. The most significant increase in potency was obtained with the introduction of a .beta.-phenylethyl group at the P1' position, suggesting a small hydrophobic channel into the S1' subsite of stromelysin. Compd. I is relatively selective for rabbit stromelysin with a  $K_i = 6.5$  nM and may prove useful for elucidating the role of endogenously-produced stromelysin in lapine models of tissue degra.

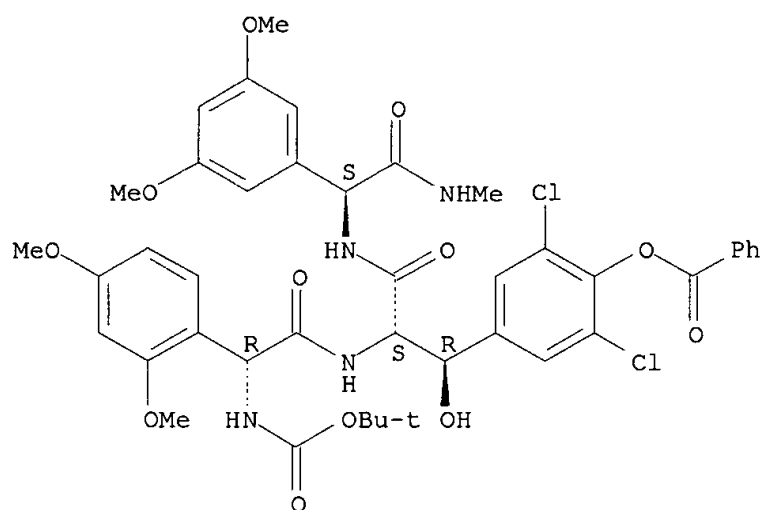
L4 ANSWER 84 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1994:271119 CAPLUS  
 DN 120:271119  
 TI Kinetic and thermodynamic atropdiastereoselection in the synthesis of the M(5-7) tripeptide portion of vancomycin  
 AU Evans, David A.; Dinsmore, Christopher J.  
 CS Dep. Chem., Harvard Univ., Cambridge, MA, 02138, USA  
 SO Tetrahedron Letters (1993), 34(38), 6029-32  
 CODEN: TELEAY; ISSN: 0040-4039  
 DT Journal  
 LA English  
 IT **154578-63-9 154578-65-1 154578-67-3**  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (cyclization of, stereochem. of vanadium oxyfluoride-promoted)  
 RN 154578-63-9 CAPLUS  
 CN Glycinamide, N-acetyl-D-2-(2,4-dimethoxyphenyl)glycyl-O-benzoyl-3,5-dichloro-threo-.beta.-hydroxy-L-tyrosyl-L-2-(3,5-dimethoxyphenyl)-N-methyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 154578-65-1 CAPLUS  
 CN Glycinamide, D-2-(2,4-dimethoxyphenyl)-N-[(1,1-dimethylethoxy)carbonyl]glycyl-O-benzoyl-3,5-dichloro-threo-.beta.-hydroxy-L-tyrosyl-L-2-(3,5-dimethoxyphenyl)-N-methyl- (9CI) (CA INDEX NAME)

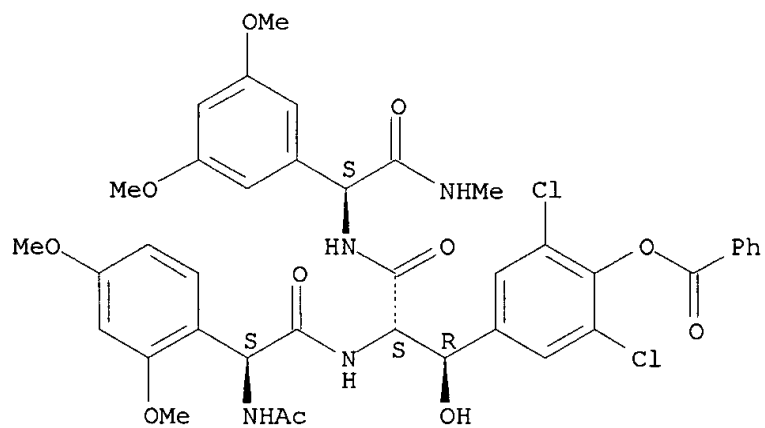
Absolute stereochemistry.



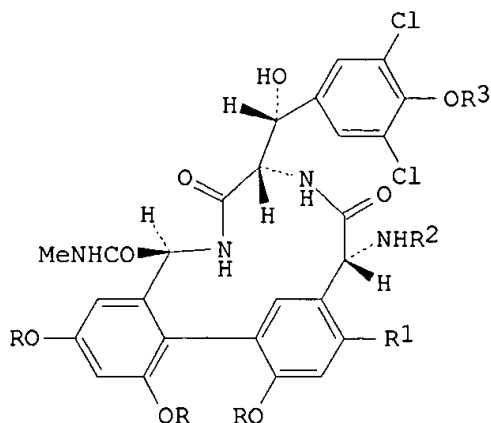
RN 154578-67-3 CAPLUS

CN Glycinamide, N-acetyl-L-2-(2,4-dimethoxyphenyl)glycyl-O-benzoyl-3,5-dichloro-threo-.beta.-hydroxy-L-tyrosyl-L-2-(3,5-dimethoxyphenyl)-N-methyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB The C.alpha. stereochem. of the position-5 arylglycine plays a pivotal role in detg. the kinetic atropdiastereoselection in the oxidative biaryl cyclization reaction, they key step in a biomimetic strategy directed toward the synthesis of the M(5-7) vancomycin fragment I. The equil. ratio of biaryl and amide conformations within the 12-membered macrocycle is significantly influenced by interaction of this same center with adjacent substituents.

L4 ANSWER 85 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1994:244406 CAPLUS

DN 120:244406

TI Semisynthetic .beta.-lactam antibiotics. Synthesis and antibacterial activity of 6.beta.-[(R)-2-((3,4-disubstituted phenyl)-alkanecarboxyamido)phenylacetamido]penicillanic acids

AU Tsou, Tai Li; Ho, Su Neng; Chang, Li Ren

CS Inst. Prevent. Med., Natl. Def. Med. Cent., Taipei, Taiwan

SO Zhonghua Yaoxue Zazhi (1993), 45(6), 563-72

CODEN: CYHCEX; ISSN: 1016-1015

DT Journal

LA English

IT 21488-22-2P 154315-81-8P 154315-82-9P

154315-83-0P 154315-84-1P 154315-86-3P

154315-87-4P 154315-88-5P 154315-89-6P

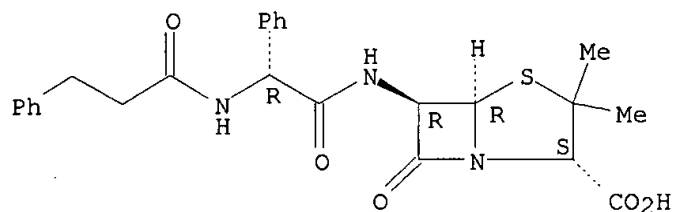
154315-90-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. and bactericidal activity of)

RN 21488-22-2 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 3,3-dimethyl-7-oxo-6-[[[(1-oxo-3-phenylpropyl)amino]phenylacetyl]amino]-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

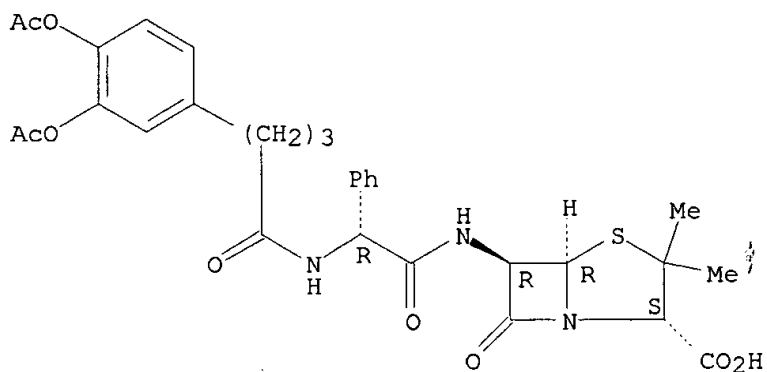
Absolute stereochemistry.



RN 154315-81-8 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[4-[3,4-bis(acetyloxy)phenyl]-1-oxobutyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

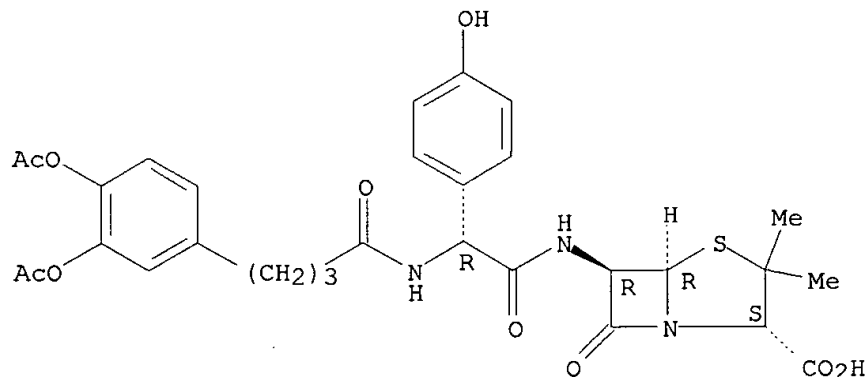
Absolute stereochemistry.



RN 154315-82-9 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[4-[3,4-bis(acetyloxy)phenyl]-1-oxobutyl]amino](4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

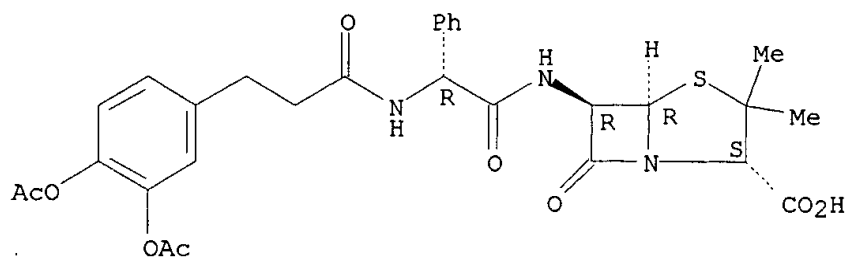


RN 154315-83-0 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[3-[3,4-bis(acetyloxy)phenyl]-1-oxopropyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-

oxo-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

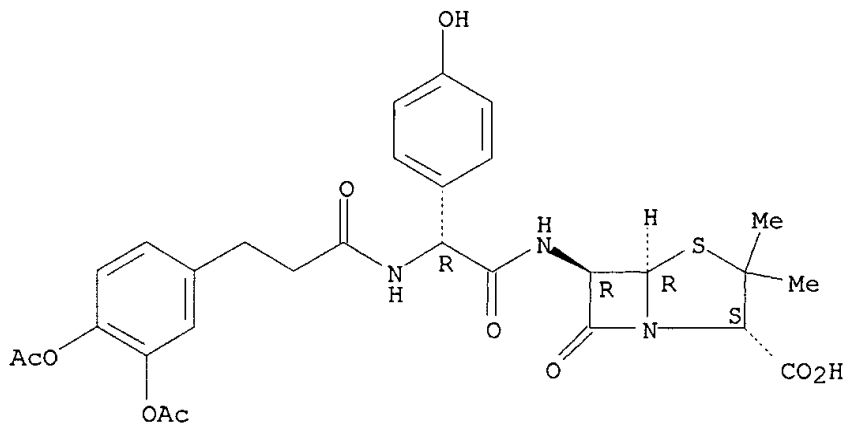
Absolute stereochemistry.



RN 154315-84-1 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[3-[3,4-bis(acetyloxy)phenyl]-1-oxopropyl]amino](4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

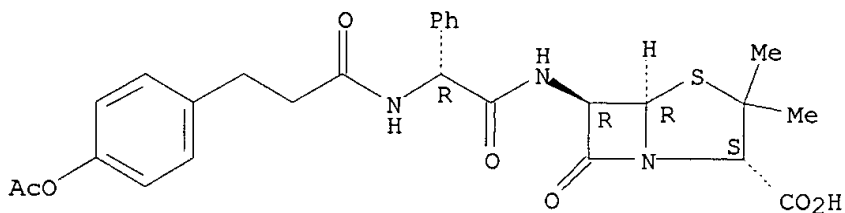
Absolute stereochemistry.



RN 154315-86-3 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[3-[4-(acetyloxy)phenyl]-1-oxopropyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

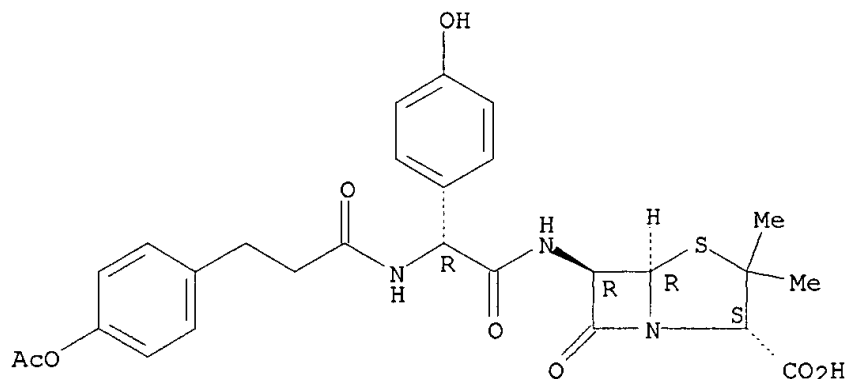
Absolute stereochemistry.



RN 154315-87-4 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[3-[4-(acetyloxy)phenyl]-1-oxopropyl]amino](4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

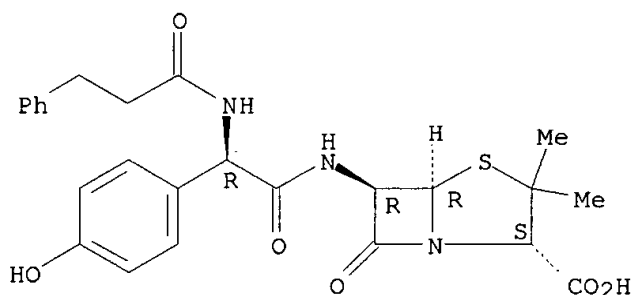
Absolute stereochemistry.



RN 154315-88-5 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[4-hydroxyphenyl][(1-oxo-3-phenylpropyl)amino]acetyl]amino]-3,3-dimethyl-7-oxo-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

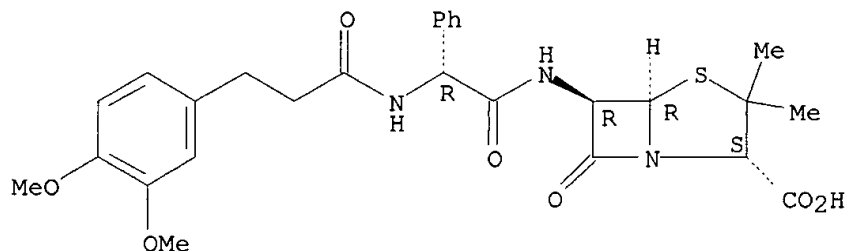
Absolute stereochemistry.



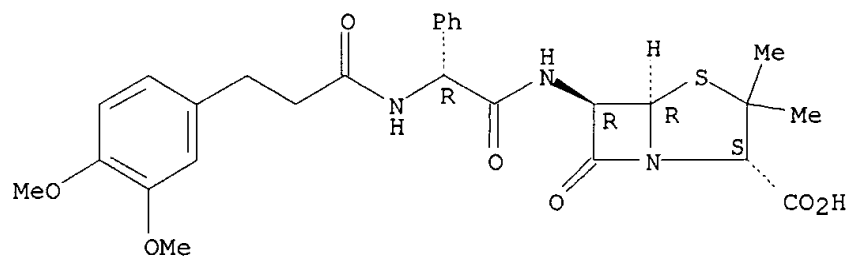
RN 154315-89-6 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[3-(3,4-dimethoxyphenyl)-1-oxopropyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



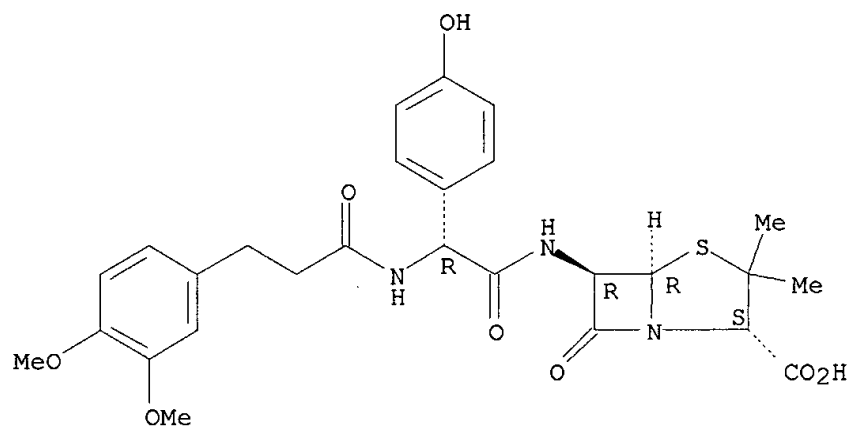




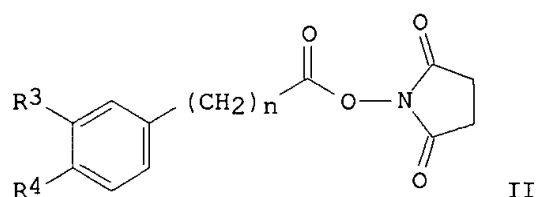
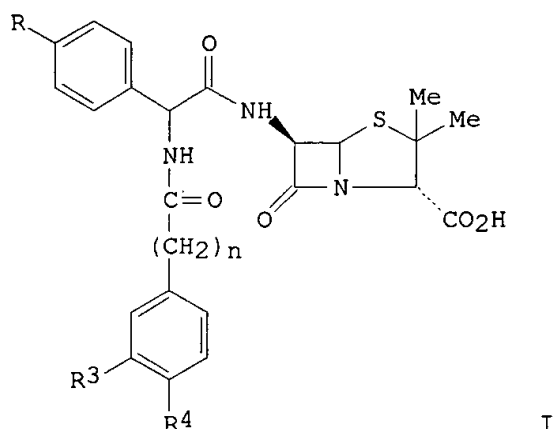
RN 154315-90-9 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[3-(3,4-dimethoxyphenyl)-1-oxopropyl]amino](4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB In order to improve the antibacterial activity, a series of 6.beta.-[(R)-.alpha.-amino-phenylacetamido]penicillanic acids I (R = H, OH, R3, R4 = OAc, H, OMe, n = 0-3) with various substituents at the .alpha.-amino group were prepd. by reacting ampicillin or amoxicillin with N-succinamido-substituted phenylalkanes II. Structures of these products were detd. by 1H NMR, FAB-MS, and FT-IR spectral analyses. In comparison with the parent drugs, I (R3 = R4 = OAc, n = 0-3), having a [(diacetoxyphenyl)alkyl]carbonyl group, are active in vitro against gram pos. and gram neg. bacteria, including *Pseudomonas aeruginosa*. The other compds., I (R3 = H, R4 = OAc, n = 2; R3 = R4 = OMe, n = 2) displayed activity only in *Staphylococcus* and *Streptococcus* strains. For the .beta.-lactamase producing strains, all of the derivs. are inferior to the parents. The structure activity relationships of these derivs. indicated some facts. First, compds. with increasing no. of carbon atoms between the diacetoxyphenyl moiety and .alpha.-amino group of ampicillin or amoxicillin would retain the potency against all the tested strains. Second, compds. with increasing lipophilicity of the side chains exhibited less activity against gram neg. bacteria.

L4 ANSWER 86 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1994:134999 CAPLUS

DN 120:134999

TI HIV-1 protease inhibitors: synthesis and biological evaluation of glycopeptide mimetics

AU Ghosh, Arun K.; McKee, Sean P.; Sanders, William M.; Darke, Paul L.; Zugay, Joan A.; Emini, Emilio A.; Schleif, William A.; Quintero, Julio C.; Huff, Joel R.; Anderson, Paul S.

CS Dep. Med. Chem., Mol. Biol., Merck Research Lab., West Point, PA, 19486, USA

SO Drug Design and Discovery (1993), 10(1), 77-88  
CODEN: DDDIEV; ISSN: 1055-9612

DT Journal

LA English

IT 152843-94-2P 152886-93-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

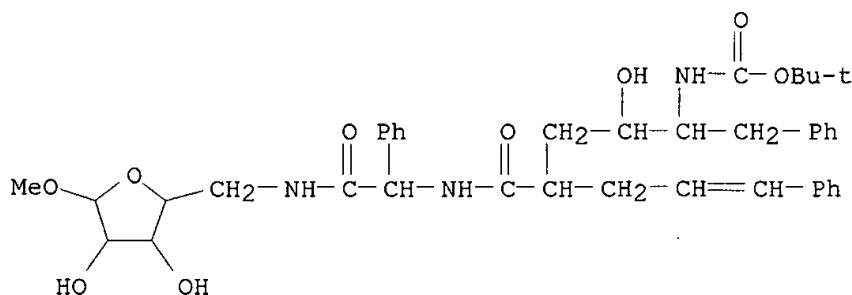
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177 (prepn. and antiviral activity of)

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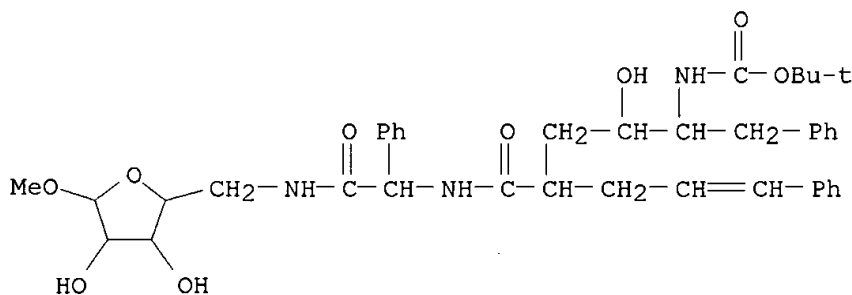
RN 152843-94-2 CAPLUS

CN .beta.-D-Xylofuranoside, methyl 5-deoxy-5-[[[[5-[[[1,1-dimethylethoxy)carbonyl]amino]-4-hydroxy-1-oxo-6-phenyl-2-(3-phenyl-2-propenyl)hexyl]amino]phenylacetyl]amino]-, [2R-[1(S\*),2R\*,4S\*,5S\*]]- (9CI)  
(CA INDEX NAME)

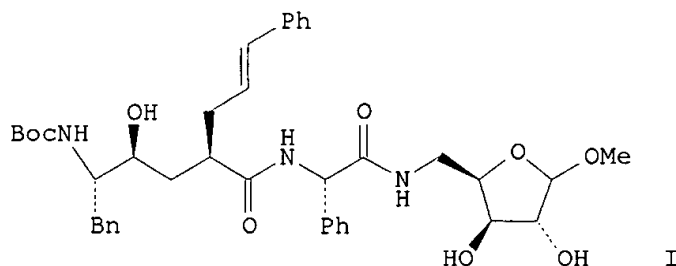


RN 152886-93-6 CAPLUS

CN .alpha.-D-Xylofuranoside, methyl 5-deoxy-5-[[[5-[[1,1-dimethylethoxy) carbonyl] amino]-4-hydroxy-1-oxo-6-phenyl-2-(3-phenyl-2-propenyl) hexyl] amino] phenylacetyl] amino]-, [2R-[1(S\*),2R\*(E),4S\*,5S\*)]-(9CI) (CA INDEX NAME)



GI



AB A series of glycopeptide mimetics, e.g. I, based on the hydroxyethylene Phe-Phe isostere have been synthesized and evaluated for their ability to inhibit the enzyme HIV-1 protease. Within this series, compd. I was the most potent inhibitor (ED<sub>50</sub> value 0.17 nM). This compd. has also shown to block the spread of HIV-1 in T-lymphoid cells at an inhibitor concn. of 200 nM.

L4 ANSWER 87 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1993:670782 CAPLUS

DN 119:270782

TI Preparation of acyclic ethylenediamine derivatives as substance P receptor antagonists

IN O'Neill, Brian T.

PA Pfizer Inc., USA

SO PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO.  | DATE     |
|----|--|------|----------|------------------|----------|
| PI | WO 9310073   | A1   | 19930527 | WO 1992-US7730   | 19920918 |
|    | W: AU, CA, FI, HU, JP, KR, NO, US                              |      |          |                  |          |
|    | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE |      |          |                  |          |
|    | AU 9226813   | A1   | 19930615 | AU 1992-26813    | 19920918 |
|    |  |      |          | US 1991-790934 A | 19911112 |
|    |  |      |          | WO 1992-US7730 A | 19920918 |
|    | EP 613458  | A1   | 19940907 | EP 1992-921029   | 19920918 |
|    | EP 613458  | B1   | 19980107 |                  |          |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE  |      |          |                  |          |
|    |  |      |          | US 1991-790934 A | 19911112 |
|    |  |      |          | WO 1992-US7730 W | 19920918 |
|    | JP 06510792  | T2   | 19941201 | JP 1992-509229   | 19920918 |
|    | JP 2614408   | B2   | 19970528 |                  |          |
|    |  |      |          | US 1991-790934 A | 19911112 |
|    |  |      |          | WO 1992-US7730 W | 19920918 |
|    | HU 70741   | A2   | 19951030 | HU 1994-1337     | 19920918 |
|    |  |      |          | US 1991-790934 A | 19911112 |
|    | AT 161821  | E    | 19980115 | AT 1992-921029   | 19920918 |
|    |  |      |          | US 1991-790934 A | 19911112 |
|    | ES 2111650   | T3   | 19980316 | ES 1992-921029   | 19920918 |
|    |  |      |          | US 1991-790934 A | 19911112 |
|    | CA 2324959   | C    | 20021112 | CA 1992-2324959  | 19920918 |
|    |  |      |          | US 1991-790934 A | 19911112 |

|               |   |          |                           |
|---------------|---|----------|---------------------------|
| ZA 9208682    | A | 19940511 | CA 1992-2123403A319920918 |
| FI 9402187    | A | 19940511 | ZA 1992-8682 19921111     |
|               |   |          | US 1991-790934 A 19911112 |
| NO 9401784    | A | 19940511 | FI 1994-2187 19940511     |
|               |   |          | US 1991-790934 A 19911112 |
| US 5521220    | A | 19960528 | WO 1992-US7730 W 19920918 |
|               |   |          | NO 1994-1784 19940511     |
|               |   |          | US 1991-790934 A 19911112 |
|               |   |          | WO 1992-US7730 A 19920918 |
|               |   |          | US 1994-240657 19940720   |
|               |   |          | US 1991-790934 B219911112 |
| FI 2001000083 | A | 20010115 | WO 1992-US7730 W 19920918 |
|               |   |          | FI 2001-83 20010115       |
|               |   |          | US 1991-790934 A 19911112 |
|               |   |          | WO 1992-US7730 W 19920918 |

## PATENT FAMILY INFORMATION:

FAN 1996:380219

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO.           | DATE     |
|----|--|------|----------|---------------------------|----------|
| PI | US 5521220   | A    | 19960528 | US 1994-240657            | 19940720 |
|    |  |      |          | US 1991-790934 B219911112 |          |
|    |  |      |          | WO 1992-US7730 W 19920918 |          |
|    | WO 9310073   | A1   | 19930527 | WO 1992-US7730            | 19920918 |
|    | W: AU, CA, FI, HU, JP, KR, NO, US                              |      |          |                           |          |
|    | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE |      |          |                           |          |
|    | CA 2324959   | C    | 20021112 | US 1991-790934 A219911112 |          |
|    |  |      |          | CA 1992-2324959           | 19920918 |
|    |  |      |          | US 1991-790934 A 19911112 |          |
|    |  |      |          | CA 1992-2123403A319920918 |          |

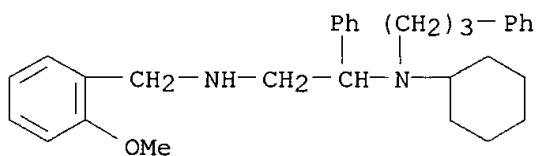
OS CASREACT 119:270782; MARPAT 119:270782

IT **150917-46-7P**

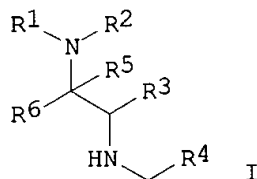
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, as substance P receptor antagonist)

RN 150917-46-7 CAPLUS

CN 1,2-Ethanediamine, N1-cyclohexyl-N2-[(2-methoxyphenyl)methyl]-1-phenyl-N1-(3-phenylpropyl)- (9CI) (CA INDEX NAME)



GI



AB Title compds. [I; R1 = H, C1-8 alkyl, C6-10 carbocyclic two-fused-ring system or a bridged two ring system, benzyl, substituted benzyl; R2 = H, benzyl, R(CH<sub>2</sub>)<sub>m</sub> (m = 0-12), the chain may contain C=C or C.tplbond.C bonds and may be substituted; R1R2N = C3-8 satd. or unsatd. heterocycle, or a fused or bridged heterocyclic system; R3 = H, C3-8 cycloalkyl, C1-6 (un)branched alkyl, (un)substituted Ph, or fluoroalkylphenyl or fluoroalkoxy; R4, R5 = aryl (e.g., Ph, naphthyl, or heteroaryl; R5 = H, alkyl, Ph, or alkyl- or alkoxyphenyl which may be fluorinated in the side chain; R6 = H, (un)branched alkyl, cycloalkyl, aryl, heteroaryl], useful as substance P receptor antagonists (no data), are prepd. Thus, aq. NaHSO<sub>3</sub> was treated with PHCHO-MeOH and then cyclohexylamine and KCN to give 79.6% .alpha.-cyclohexylaminobenzeneacetonitrile which was reduced by DIBAL in PhMe to give 74% 1-N-cyclohexyl-1-phenyl-1,2-ethanediamine. This diamine in HOAc contg. 3 .ANG. mol. sieves was treated with anisaldehyde and Na(AcO)3BH to give 41% 1-N-cyclohexyl-1-phenyl-2-N'[(2-methoxyphenyl)methyl]-1,2-ethanediamine.

L4 ANSWER 88 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1993:603857 CAPLUS

DN 119:203857

TI Preparation of modified peptides transportable into the central nervous system

IN Arvantis, Argyrios; Cain, Gary Avonn; Christos, Thomas Eugene; Confalone, Pasquale Nicholas; Pottorf, Richard Scott; Schmidt, William Koch

PA Du Pont Merck Pharmaceutical Co., USA

SO PCT Int. Appl., 111 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|----|--|------|----------|-----------------|----------|
| PI | WO 9300359   | A1   | 19930107 | WO 1992-US4968  | 19920618 |
|    | W: AU, CA, JP  |      |          |                 |          |
|    | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE |      |          |                 |          |
|    |  |      |          | US 1991-723616  | 19910627 |
|    | AU 9222381   | A1   | 19930125 | AU 1992-22381   | 19920618 |
|    |  |      |          | US 1991-723616  | 19910627 |
|    |  |      |          | WO 1992-US4968  | 19920618 |

OS MARPAT 119:203857

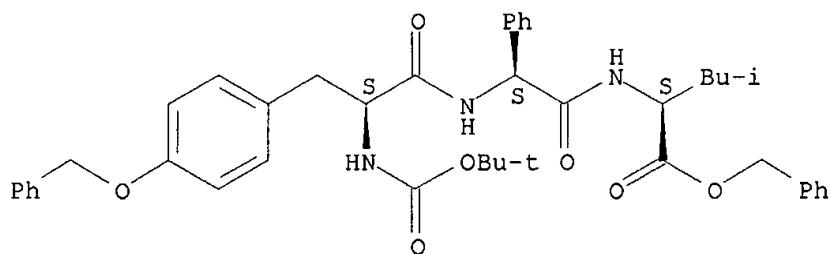
IT **150435-49-7P 150435-50-0P 150435-51-1P**  
**150435-52-2P 150435-53-3P 150463-78-8P**  
**150463-79-9P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as intermediate for neurotensin analog)

RN 150435-49-7 CAPLUS

CN L-Leucine, N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-tyrosyl]-L-2-phenylglycyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

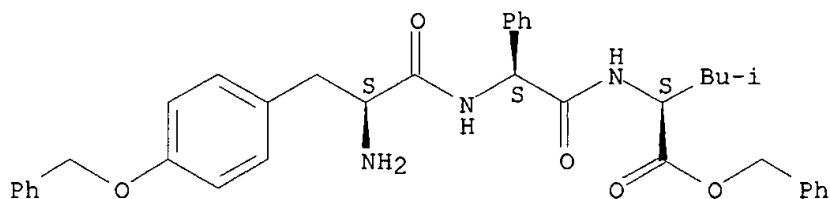
Absolute stereochemistry.



RN 150435-50-0 CAPLUS

CN L-Leucine, N-[L-2-phenyl-N-[O-(phenylmethyl)-L-tyrosyl]glycyl]-, phenylmethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

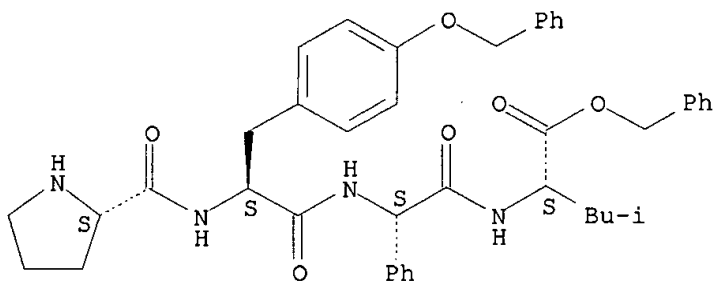


● HCl

RN 150435-51-1 CAPLUS

CN L-Leucine, N-[L-2-phenyl-N-[O-(phenylmethyl)-N-L-prolyl-L-tyrosyl]glycyl]-, phenylmethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

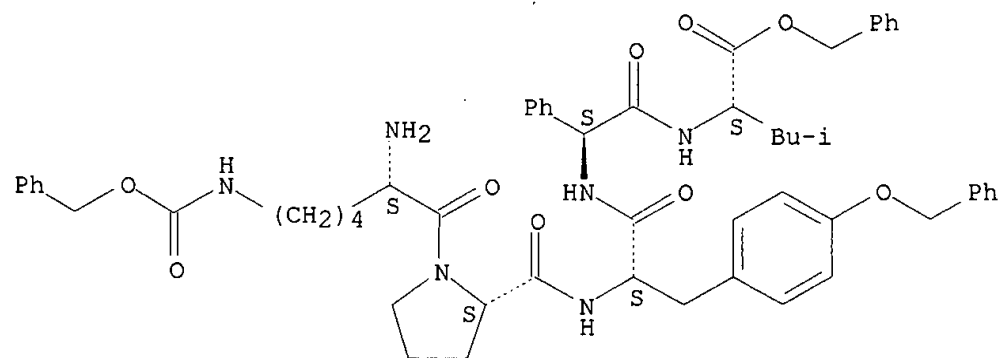


● HCl

RN 150435-52-2 CAPLUS

CN L-Leucine, N-[L-2-phenyl-N-[N-[1-[N6-[(phenylmethoxy)carbonyl]-L-lysyl]-L-prolyl]-O-(phenylmethyl)-L-tyrosyl]glycyl]-, phenylmethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

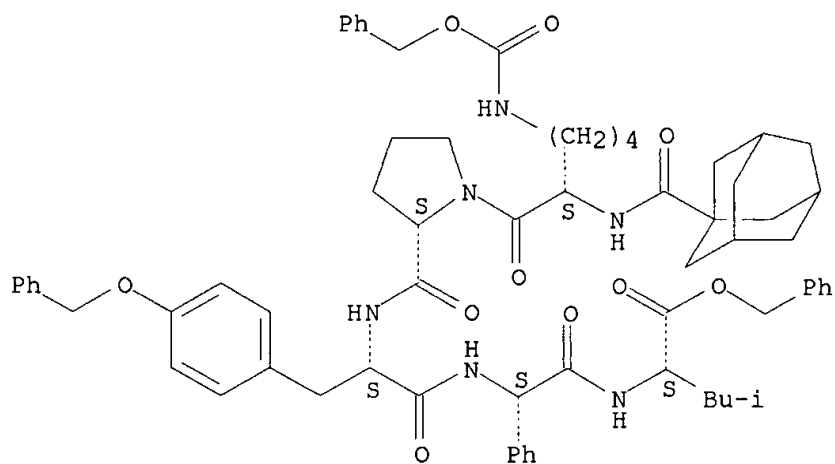


● HCl

RN 150435-53-3 CAPLUS

CN L-Leucine, N-[L-2-phenyl-N-[N-[1-[N6-[(phenylmethoxy)carbonyl]-N2-(tricyclo[3.3.1.13,7]dec-1-ylcarbonyl)-L-lysyl]-L-prolyl]-O-(phenylmethyl)-L-tyrosyl]glycyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

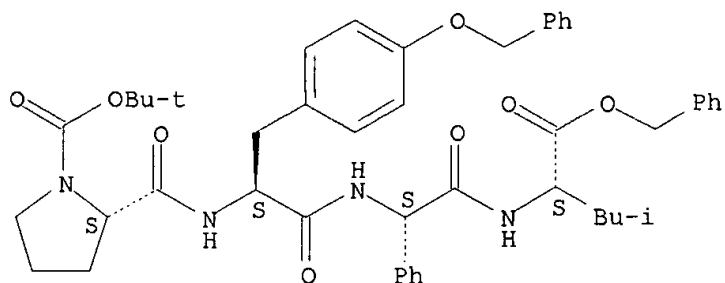


RN 150463-78-8 CAPLUS

CN L-Leucine, N-[N-[N-[1-[(1,1-dimethylethoxy)carbonyl]-L-prolyl]-O-(phenylmethyl)-L-tyrosyl]-L-2-phenylglycyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



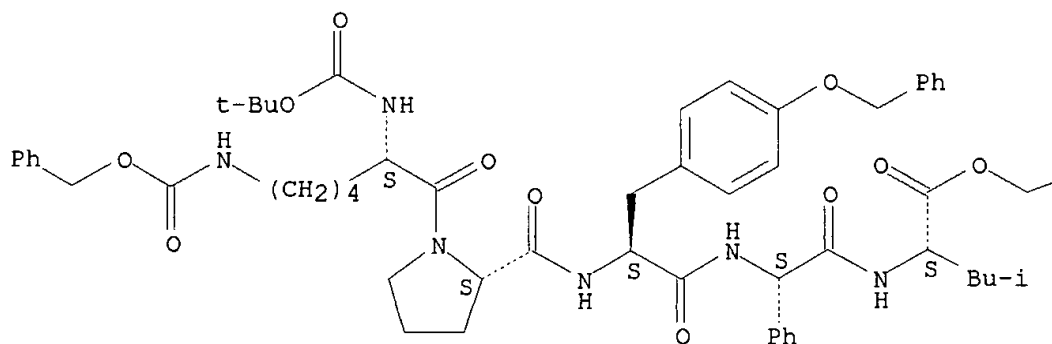


RN 150463-79-9 CAPLUS

CN L-Leucine, N-[N-[N-[1-[N2-[(1,1-dimethylethoxy) carbonyl]-N6-[(phenylmethoxy) carbonyl]-L-lysyl]-L-prolyl]-O-(phenylmethyl)-L-tyrosyl]-L-2-phenylglycyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

— Ph

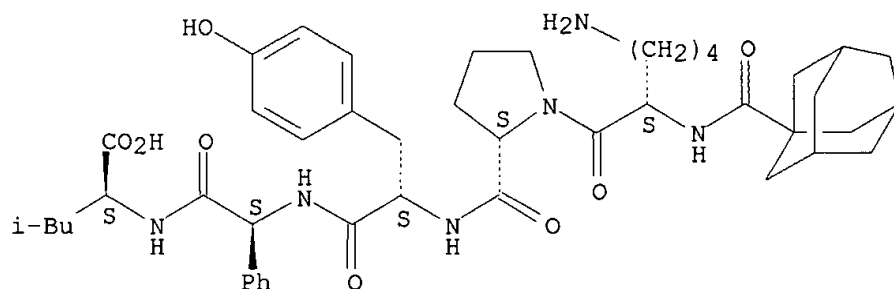
IT 150434-66-5P 150434-67-6P 150435-05-5P  
150435-92-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as neurotensin analog)

RN 150434-66-5 CAPLUS

CN L-Leucine, N-[L-2-phenyl-N-[N-[1-[N2-(tricyclo[3.3.1.3<sup>0</sup>.3<sup>1</sup>.3<sup>2</sup>]-dec-1-ylcarbonyl]-L-lysyl]-L-prolyl]-L-tyrosyl]glycyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 150434-67-6 CAPLUS

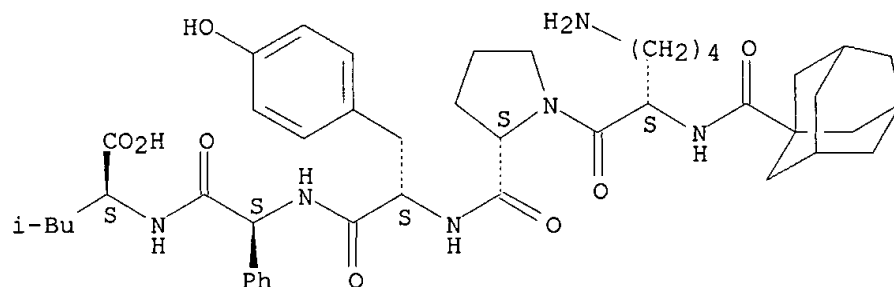
CN L-Leucine, N-[L-2-phenyl-N-[N-[1-[N2-(tricyclo[3.3.1.1.3,7]dec-1-ylcarbonyl)-L-lysyl]-L-prolyl]-L-tyrosyl]glycyl]-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 150434-66-5

CMF C45 H62 N6 O8

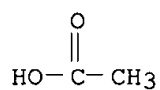
Absolute stereochemistry.



CM 2

CRN 64-19-7

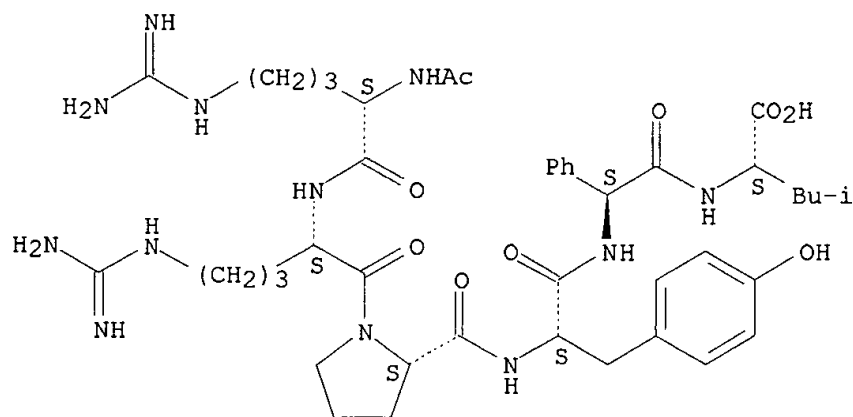
CMF C2 H4 O2



RN 150435-05-5 CAPLUS

CN L-Leucine, N-[N-[N-[1-[N2-(N2-acetyl-L-arginyl)-L-arginyl]-L-prolyl]-L-tyrosyl]-L-2-phenylglycyl]- (9CI) (CA INDEX NAME)

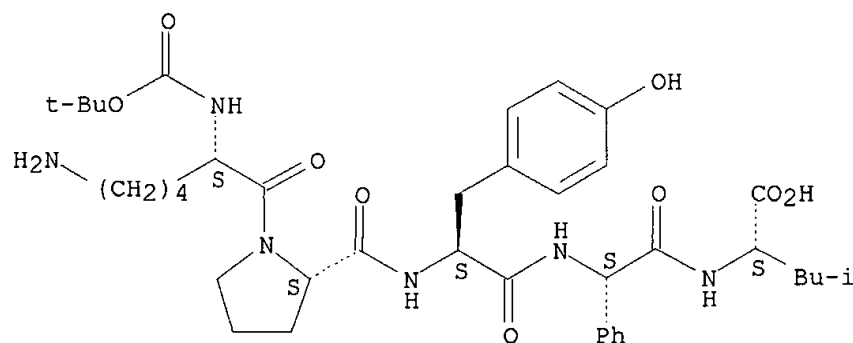
Absolute stereochemistry.



RN 150435-92-0 CAPLUS

CN L-Leucine, N-[N-[N-[1-[N2-[(1,1-dimethylethoxy)carbonyl]-L-lysyl]-L-prolyl]-L-tyrosyl]-L-2-phenylglycyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB YWmXnA1-H-A-B-C-D-E-F-Z [Y = lipophilic moiety LCO, R(CH<sub>2</sub>)<sub>p</sub> (O(CH<sub>2</sub>)<sub>r</sub>); p, r = 0-6; L = (substituted) alkyl, perfluoroalkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, etc.; R = cycloalkyl, heterocyclyl, (substituted) aryl; W = Arg, D-Arg, D-Lys, Pro, Nle, Lys, Orn, homoarginine, 2,4-diaminobutyric acid, 2,3-diaminopropionic acid, N-methylnorleucine, 4-aminocyclohexylalanine residues; X = W, Ala, etc.; m, n = 0,1; A, A1, C, E = CONH, CONMe, NMeCO, CH<sub>2</sub>NH, CH<sub>2</sub>O, CH<sub>2</sub>S, CSNH, NHCONH, SOCH<sub>2</sub>, SO<sub>2</sub>CH<sub>2</sub>, NHSC, CH:CH, CH<sub>2</sub>CH<sub>2</sub>, CF<sub>2</sub>CF<sub>2</sub>, CF:CF, CF:CH, CH<sub>2</sub>CH(OH), cyclopropylene, 4,5-tetrazolyldiyl, etc.; H = Pro, N-methylaminobutyric acid residue; B = Tyr, Phe, Trp, naphthylalanine, phenylglycine, .beta.-phenylproline residues; D = Ile, Leu, tert-leucine, phenylglycine residues; F = Leu, Val, Met; Z = OH, alkoxy], were prepd. Thus, Q-Arg-Pro-Tyr-Ile-Leu-OH.HOAC (Q = 1-adamantanecarbonyl), prepd. by solid phase coupling on phenylacetamidomethyl resin using BOC-protected amino acids and DCC/1-hydroxybenzotriazole, showed K<sub>i</sub> = 144 nM in a neurotensin binding assay and ED<sub>50</sub> = 14 mg/kg i.v. in the phenylquinone writhing test in mice.

L4 ANSWER 89 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1993:539766 CAPLUS

DN 119:139766

TI Oxidative coupling of arylglycine-containing peptides. A biomimetic approach to the synthesis of the macrocyclic actinoidinic-containing vancomycin subunit

AU Evans, David A.; Dinsmore, Christopher J.; Evrard, Deborah A.; DeVries, Keith M.

CS Dep. Chem., Harvard Univ., Cambridge, MA, 02138, USA

SO Journal of the American Chemical Society (1993), 115(14), 6426-7  
CODEN: JACSAT; ISSN: 0002-7863

DT Journal

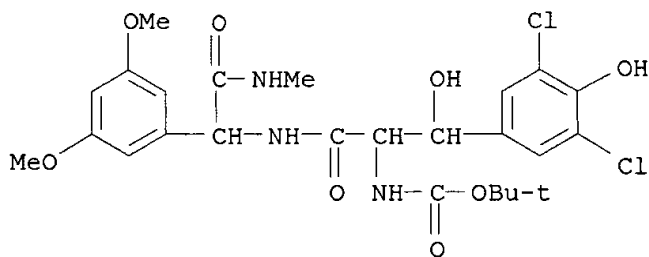
LA English

OS CASREACT 119:139766

IT **149623-79-0P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and benzylation of)

RN 149623-79-0 CAPLUS

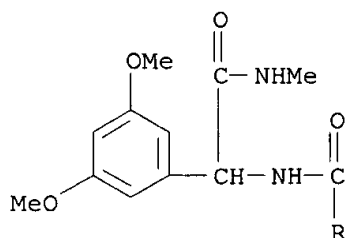
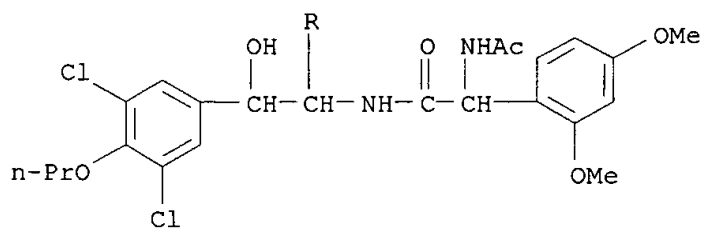
CN Glycinamide, 3,5-dichloro-N-[(1,1-dimethylethoxy)carbonyl]-threo-.beta.-hydroxy-L-tyrosyl-L-2-(3,5-dimethoxyphenyl)-N-methyl- (9CI) (CA INDEX NAME)



IT **149623-51-8P 149623-52-9P 149623-69-8P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and intramol. oxidative biaryl coupling of, with vanadium oxyfluoride)

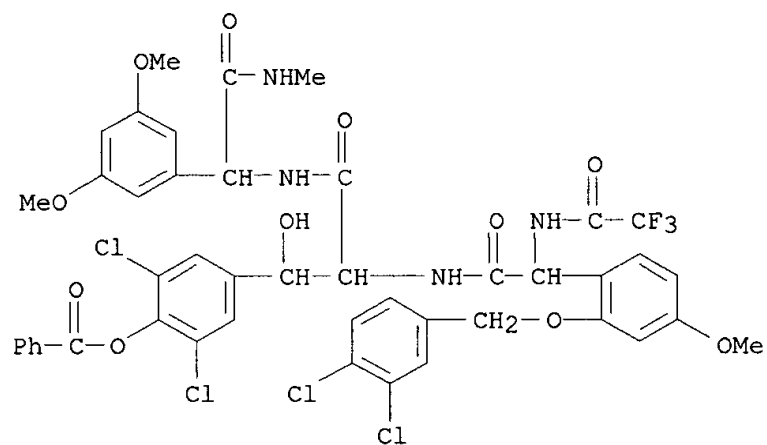
RN 149623-51-8 CAPLUS

CN Glycinamide, N-acetyl-D-2-(2,4-dimethoxyphenyl)glycyl-3,5-dichloro-threo-.beta.-hydroxy-O-propyl-L-tyrosyl-L-2-(3,5-dimethoxyphenyl)-N-methyl- (9CI) (CA INDEX NAME)



RN 149623-52-9 CAPLUS

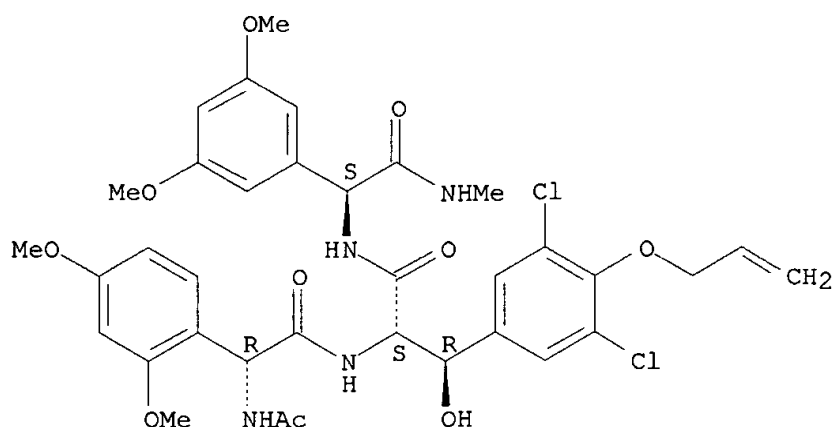
CN Glycinamide, D-2-[2-[(3,4-dichlorophenyl)methoxy]-4-methoxyphenyl]-N-(trifluoroacetyl)glycyl-O-benzoyl-3,5-dichloro-threo-.beta.-hydroxy-L-tyrosyl-L-2-(3,5-dimethoxyphenyl)-N-methyl- (9CI) (CA INDEX NAME)



RN 149623-69-8 CAPLUS

CN Glycinamide, N-acetyl-D-2-(2,4-dimethoxyphenyl)glycyl-3,5-dichloro-threo-.beta.-hydroxy-O-2-propenyl-L-tyrosyl-L-2-(3,5-dimethoxyphenyl)-N-methyl- (9CI) (CA INDEX NAME)

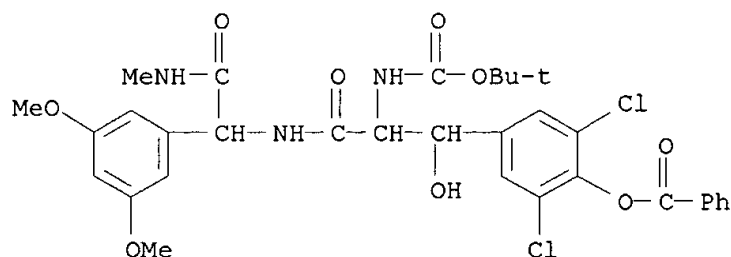
Absolute stereochemistry.

IT **149623-80-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and peptide coupling of, with arylglycine deriv., in prepn. of vancomycin fragment)

RN 149623-80-3 CAPLUS

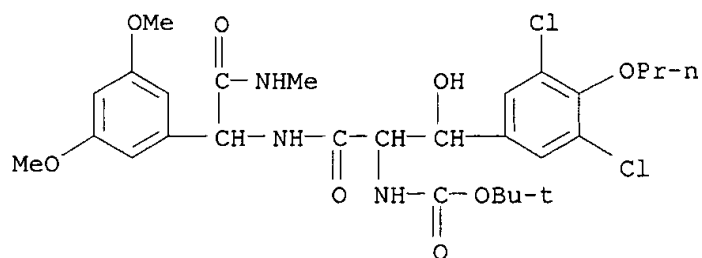
CN Glycinamide, O-benzoyl-3,5-dichloro-N-[(1,1-dimethylethoxy)carbonyl]-threo-.beta.-hydroxy-L-tyrosyl-L-2-(3,5-dimethoxyphenyl)-N-methyl- (9CI) (CA INDEX NAME)

IT **149623-66-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and peptide coupling of, with arylglycine deriv., in prepn. of vancomycin fragment model)

RN 149623-66-5 CAPLUS

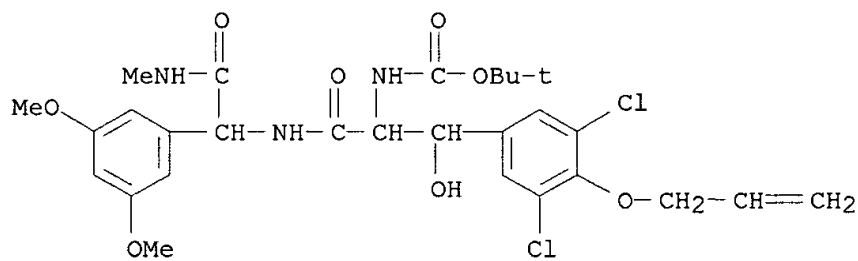
CN Glycinamide, 3,5-dichloro-N-[(1,1-dimethylethoxy)carbonyl]-threo-.beta.-hydroxy-O-propyl-L-tyrosyl-L-2-(3,5-dimethoxyphenyl)-N-methyl- (9CI) (CA INDEX NAME)

IT **149623-65-4P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn., catalytic hydrogenation, or deallylation of)

RN 149623-65-4 CAPLUS

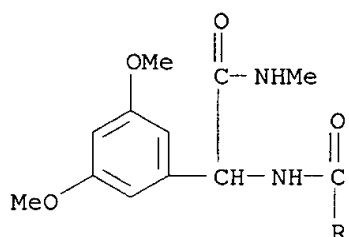
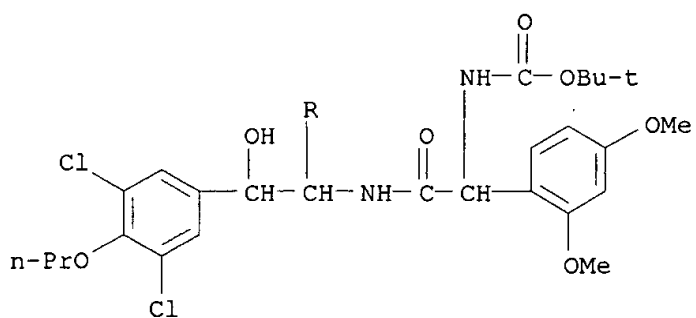
CN Glycinamide, (.beta.R)-3,5-dichloro-N-[(1,1-dimethylethoxy)carbonyl]-  
.beta.-hydroxy-O-2-propenyl-L-tyrosyl-(2S)-2-(3,5-dimethoxyphenyl)-N-  
methyl- (9CI) (CA INDEX NAME)

IT **149623-67-6P 149623-68-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn., deblocking, and acetylation of)

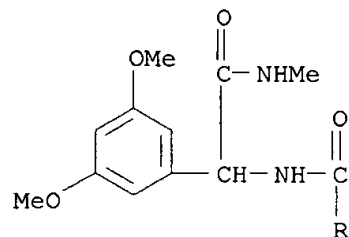
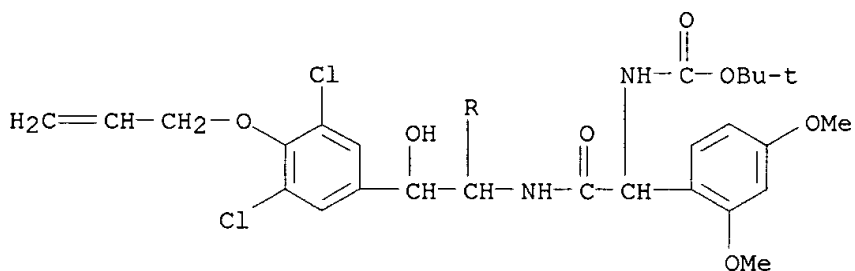
RN 149623-67-6 CAPLUS

CN Glycinamide, D-2-(2,4-dimethoxyphenyl)-N-[(1,1-  
dimethylethoxy)carbonyl]glycyl-3,5-dichloro-threo-.beta.-hydroxy-O-propyl-  
L-tyrosyl-L-2-(3,5-dimethoxyphenyl)-N-methyl- (9CI) (CA INDEX NAME)



RN 149623-68-7 CAPLUS

CN Glycinamide, D-2-(2,4-dimethoxyphenyl)-N-[(1,1-dimethylethoxy)carbonyl]glycyl-3,5-dichloro-threo-.beta.-hydroxy-O-2-propenyl-L-tyrosyl-L-2-(3,5-dimethoxyphenyl)-N-methyl- (9CI) (CA INDEX NAME)



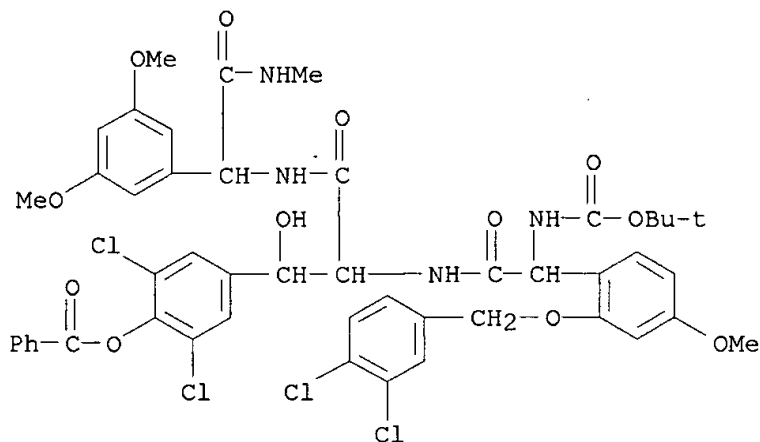
IT 149623-81-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn., deblocking, and trifluoroacetylation of)

RN 149623-81-4 CAPLUS



CN Glycinamide, D-2-[2-[(3,4-dichlorophenyl)methoxy]-4-methoxyphenyl]-N-[(1,1-dimethylethoxy)carbonyl]glycyl-O-benzoyl-3,5-dichloro-threo-.beta.-hydroxy-L-tyrosyl-L-2-(3,5-dimethoxyphenyl)-N-methyl- (9CI) (CA INDEX NAME)



GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB A biomimetic approach to the synthesis of the 12-membered cyclic tripeptide M(5-7) macrocyclic fragment I (R = R1 = H) (II), which comprises three of the seven amino acid constituents of the vancomycin aglycon is reported. The macrocyclization of the linear tripeptide precursor III to the cyclic 12-membered tripeptide I (R = OCH2C6H3Cl2-3,4, R1 = Me) was achieved by an efficient intramol. oxidative biaryl coupling with VOF3 in 64% yield. After removal of the requisite ortho phenolic residue and subsequent demethylation to the unnatural atropisomer II, atropisomerization to the M(5-7) macrocyclic tripeptide vancomycin subunit was achieved. The rotational barrier for this conformational change was 21 kcal mol<sup>-1</sup>.

L4 ANSWER 90 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1993:247987 CAPLUS

DN 118:247987

TI The action of LH-releasing hormone and five analogs on estradiol, oxytocin and vasopressin secretion by bovine granulosa cells in culture

AU Sirotkin, A. V.; Nitray, J.; Nikolajev, S. V.; Burov, S. V.

CS Dep. Exp. Endocrinol., Res. Inst. Anim. Prod., Nitra, 949 92, Czech.

SO Journal of Endocrinology (1993), 136(3), 491-6

CODEN: JOENAK; ISSN: 0022-0795

DT Journal

LA English

IT 126609-83-4

RL: BIOL (Biological study)

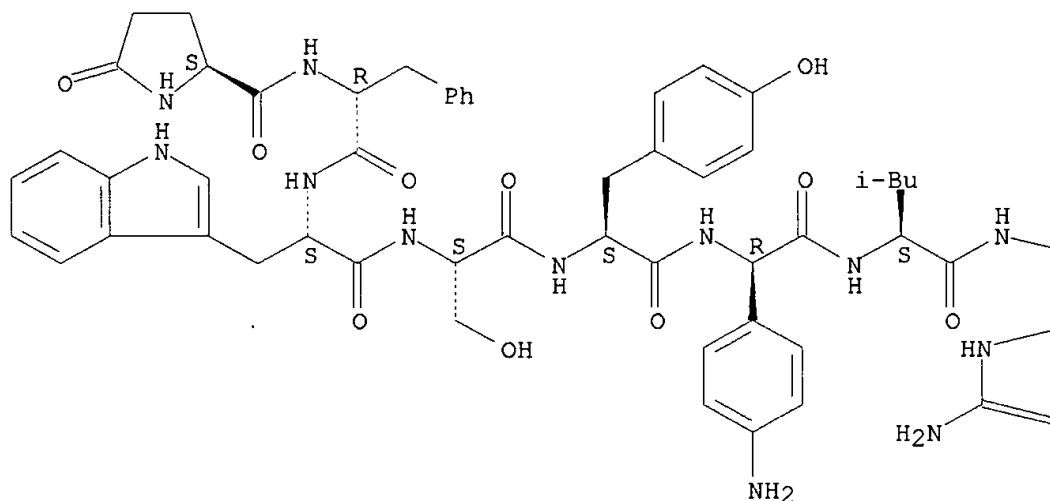
(estradiol and oxytocin and vasopressin secretion response to, in ovary granulosa cell)

RN 126609-83-4 CAPLUS

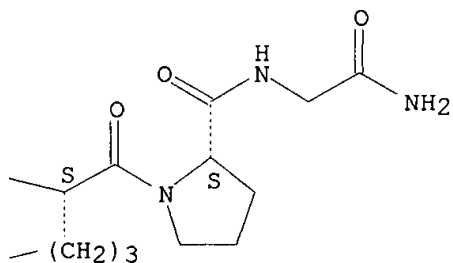
CN Luteinizing hormone-releasing factor (swine), 2-D-phenylalanine-6-(4-amino-D-phenylalanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



=NH

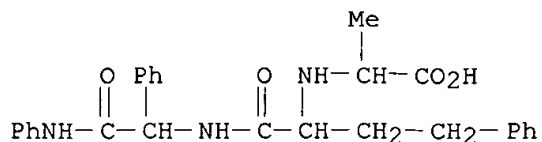
AB The release of oxytocin, AVP, and estradiol by bovine granulosa cells in culture was analyzed either with or without LH-RH, its agonists (cyclo[Prol,D-Phe6]LH-RH and de-(1-3,10)-[D-Ala6]LH-RH) or antagonists ([D-Phe2,D-Phe6]LH-RH, [D-Phe2,D-Phe(NH2)6]LH-RH, or cyclo[Prol,D-Phe2,D-Phe6]LH-RH). All preps. used stimulated granulosa oxytocin and estradiol secretion. Vasopressin release was increased after all treatments with LH-RH antagonists, but not after LH-RH or its agonists. The data demonstrate a direct influence of LH-RH and its analogs on the secretion of estrogen and nonapeptide hormones by bovine granulosa cells. A

comparison of the effects of LH-RH and its agonists and antagonists suggests that the action of these peptides at the hypophyseal and ovarian level is relatively independent.

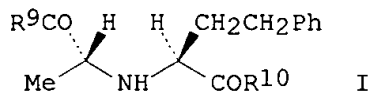
L4 ANSWER 91 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1993:234493 CAPLUS  
 DN 118:234493  
 TI Preparation of substituted N-carboxyalkylpeptidyl derivatives as  
 antidegenerative agents  
 IN Sahoo, Soumya P.; Polo, Scott A.; Durette, Philippe L.; Esser, Craig K.;  
 Hagmann, William K.; Kopka, Ihor E.; Chapman, Kevin T.; Caldwell, Charles  
 G.  
 PA Merck and Co., Inc., USA  
 SO PCT Int. Appl., 93 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|----|--|------|----------|-----------------|----------|
| PI | WO 9221360   | A1   | 19921210 | WO 1992-US3809  | 19920501 |
|    | W: CA, JP  |      |          |                 |          |
|    | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE |      |          |                 |          |
|    |  |      |          | US 1991-705826  | 19910528 |
|    |  |      |          | US 1992-873905  | 19920424 |
|    | CA 2102890   | AA   | 19921129 | CA 1992-2102890 | 19920501 |
|    |  |      |          | US 1991-705826  | 19910528 |
|    | EP 586537  | A1   | 19940316 | EP 1992-912475  | 19920501 |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE  |      |          |                 |          |
|    |  |      |          | US 1991-705826  | 19910528 |
|    |  |      |          | US 1992-873905  | 19920424 |
|    |  |      |          | WO 1992-US3809  | 19920501 |
|    | US 5932551   | A    | 19990803 | US 1997-848766  | 19970501 |
|    |  |      |          | US 1992-873905  | 19920424 |
|    |  |      |          | US 1995-397538  | 19950302 |
|    |  |      |          | US 1995-533879  | 19950926 |

OS MARPAT 118:234493  
 IT **147472-95-5P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and stromelysin, collagenase, and gelatinase inhibitory  
 activity of)  
 RN 147472-95-5 CAPLUS  
 CN Glycinamide, N-(1-carboxyethyl)-4-phenyl-L-2-aminobutanoyl-L-N,2-diphenyl-  
 , (R)- (9CI) (CA INDEX NAME)



GI



AB Title compds. R3O2CCHR1NHCH(CHR7R8)CO-AA-NR5R6 [R3 = H, C1-C10 alkyl, (un)substituted C6-C10 (hetero)aryl, (un)substituted C6-C10 (hetero)aryl-C1-C3 alkyl; R1 = C1-C6 (un)substituted alkyl; R7 = H, C1-C3 alkyl, OH; R8 = (un)substituted C6-C10 (hetero)aryl-C1-C2 alkyl; AA = amino acid residue; R5, R6 = independently H, C1-C10 alkyl, C6-C10 (un)substituted (hetero)aryl, C6-C10 (un)substituted (hetero)aryl-C1-C6 alkyl] and pharmaceutically acceptable salts thereof were prepd. as inhibitors of matrix metalloendoproteinase-mediated diseases, e.g. osteoarthritis, rheumatoid arthritis, septic arthritis, tumor invasion in certain cancers, periodontal disease, corneal ulceration, proteinuria, dystrophic epidermolysis bullosa, and coronary thrombosis assocd. with atherosclerotic plaque rupture. These claimed inhibitors may also be useful in preventing the pathol. sequelae following a traumatic injury that could lead to a permanent disability, and may also have utility as a means of birth control by preventing ovulation or implantation. Thus, reductive alkylation of 10.5 g (S)-H2NCH(CH2CH2Ph)CO2CMe3.HCl by 18.1 mL MeCOCO2CH2Ph with NaBH3CN in AcOH/pyridine gave 6.40 g adduct I (R9 = CH2Ph, R10 = OCMe3) (II). Deblocking of II with HCl, coupling with H-Leu-NHPh.HCl, and catalytic hydrogenolysis gave title adduct I (R9 = H, R10 = Leu-NHPh) (III). III inhibited stromelysin, collagenase, and 72 kD gelatinase with IC50 = 0.32, 0.06, and 0.93 .mu.M, resp.

L4 ANSWER 92 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1993:116751 CAPLUS

DN 118:116751

TI Recombinant thrombin receptor, agonist and antagonist peptides, and (monoclonal) antibodies

IN Coughlin, Shaun R.; Scarborough, Robert M.

PA University of California, Oakland, USA; Cor Therapeutics, Inc.

SO PCT Int. Appl., 80 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.   | DATE     |
|----|---|------|----------|-------------------|----------|
| PI | WO 9214750  | A1   | 19920903 | WO 1992-US1312    | 19920219 |
|    | W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE |      |          |                   |          |
|    | RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG        |      |          |                   |          |
|    |   |      |          | US 1991-657769 A  | 19910219 |
|    |   |      |          | US 1991-789184 A  | 19911107 |
|    | US 5256766  | A    | 19931026 | US 1991-657769    | 19910219 |
|    | US 5688768  | A    | 19971118 | US 1991-789184    | 19911107 |
|    |   |      |          | US 1991-657769 A2 | 19910219 |
|    | AU 9214568  | A1   | 19920915 | AU 1992-14568     | 19920219 |
|    | AU 665752   | B2   | 19960118 |                   |          |
|    |   |      |          | US 1991-657769 A  | 19910219 |
|    |   |      |          | US 1991-789184 A  | 19911107 |
|    |   |      |          | WO 1992-US1312 A  | 19920219 |

EP 572553 A1 19931208 EP 1992-907700 19920219  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE  
 US 1991-657769 A 19910219  
 US 1991-789184 A 19911107  
 WO 1992-US1312 W 19920219  
 JP 06508742 T2 19941006 JP 1992-507331 19920219  
 US 1991-657769 A 19910219  
 US 1991-789184 A 19911107  
 WO 1992-US1312 W 19920219

## PATENT FAMILY INFORMATION:

FAN 1997:761604

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.   | DATE     |
|----|---|------|----------|-------------------|----------|
| PI | US 5688768  | A    | 19971118 | US 1991-789184    | 19911107 |
|    |   |      |          | US 1991-657769 A2 | 19910219 |
|    | US 5256766  | A    | 19931026 | US 1991-657769    | 19910219 |
|    | CA 2104394  | AA   | 19920820 | CA 1992-2104394   | 19920219 |
|    |   |      |          | US 1991-657769 A  | 19910219 |
|    | WO 9214750  | A1   | 19920903 | WO 1992-US1312    | 19920219 |
|    | W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE |      |          |                   |          |
|    | RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG        |      |          |                   |          |
|    |   |      |          | US 1991-657769 A  | 19910219 |
|    |   |      |          | US 1991-789184 A  | 19911107 |
|    | AU 9214568  | A1   | 19920915 | AU 1992-14568     | 19920219 |
|    | AU 665752   | B2   | 19960118 |                   |          |
|    |   |      |          | US 1991-657769 A  | 19910219 |
|    |   |      |          | US 1991-789184 A  | 19911107 |
|    |   |      |          | WO 1992-US1312 A  | 19920219 |
|    | EP 572553   | A1   | 19931208 | EP 1992-907700    | 19920219 |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE   |      |          |                   |          |
|    |   |      |          | US 1991-657769 A  | 19910219 |
|    |   |      |          | US 1991-789184 A  | 19911107 |
|    |   |      |          | WO 1992-US1312 W  | 19920219 |
|    | JP 06508742   | T2   | 19941006 | JP 1992-507331    | 19920219 |
|    |   |      |          | US 1991-657769 A  | 19910219 |
|    |   |      |          | US 1991-789184 A  | 19911107 |
|    |   |      |          | WO 1992-US1312 W  | 19920219 |
|    | US 6197541  | B1   | 20010306 | US 1993-18760     | 19930217 |
|    |   |      |          | US 1991-657769 A1 | 19910219 |
|    |   |      |          | US 1991-789184 A3 | 19911107 |
|    | US 5759994  | A    | 19980602 | US 1995-475263    | 19950607 |
|    |   |      |          | US 1991-657769 A2 | 19910219 |
|    |   |      |          | US 1991-789184 A1 | 19911107 |
|    | US 5798248  | A    | 19980825 | US 1995-485886    | 19950607 |
|    |   |      |          | US 1991-657769 A2 | 19910219 |
|    |   |      |          | US 1991-789184 A3 | 19911107 |
|    | US 5849507  | A    | 19981215 | US 1995-477362    | 19950607 |
|    |   |      |          | US 1991-657769 A2 | 19910219 |
|    |   |      |          | US 1991-789184 A3 | 19911107 |
|    | US 5856448  | A    | 19990105 | US 1995-477134    | 19950607 |
|    |   |      |          | US 1991-657769 A2 | 19910219 |
|    |   |      |          | US 1991-789184 A3 | 19911107 |
|    | US 6024936  | A    | 20000215 | US 1995-473489    | 19950607 |
|    |   |      |          | US 1991-657769 A2 | 19910219 |
|    |   |      |          | US 1991-789184 A3 | 19911107 |

OS MARPAT 118:116751

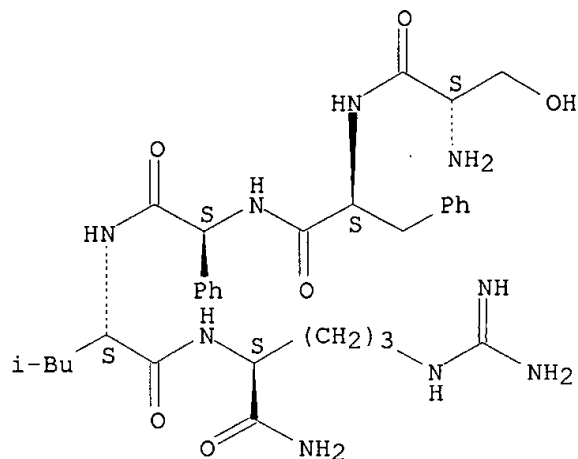
IT **145230-57-5**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(thrombin agonist activity of)

RN 145230-57-5 CAPLUS

CN L-Argininamide, L-seryl-L-phenylalanyl-(2S)-2-phenylglycyl-L-leucyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

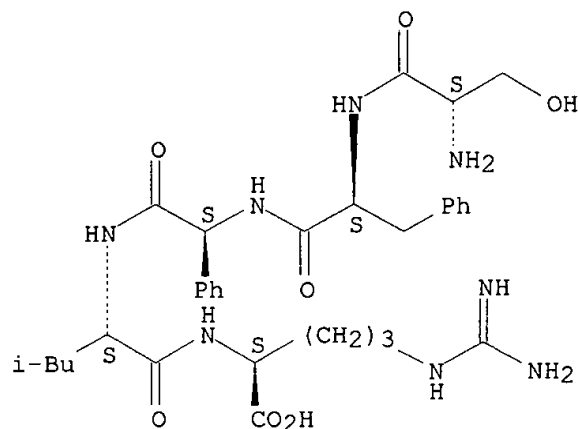
IT **145229-80-7**

RL: BIOL (Biological study)  
(thrombin receptor agonist)

RN 145229-80-7 CAPLUS

CN L-Arginine, L-seryl-L-phenylalanyl-(2S)-2-phenylglycyl-L-leucyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



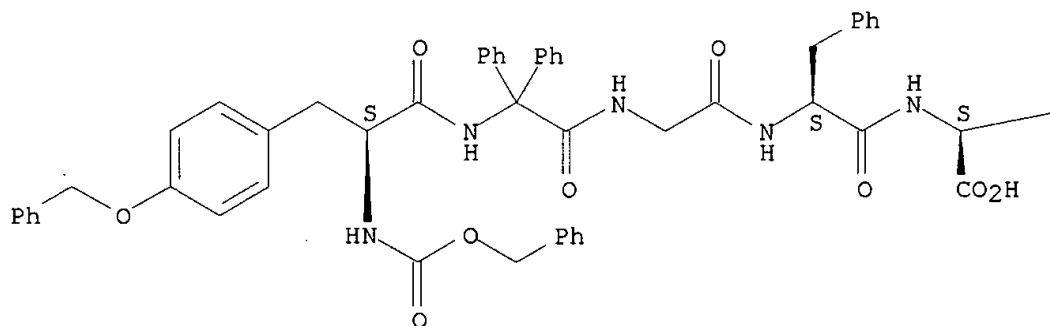
AB The DNA encoding the cell-surface receptor for thrombin has been cloned and sequenced. The availability of this DNA permits the recombinant

prodn. of thrombin receptor which can be produced at cell surfaces and is useful in assay systems both for the detection of thrombin and for the evaluation of candidate thrombin agonists and antagonists. Further, the elucidation of the thrombin receptor permits the design of agonist and antagonist compds. which are useful diagnostically and therapeutically. The availability of the thrombin receptor also permits prodn. of antibodies specifically immunoreactive with the receptor per se or with specific regions thereof which are also useful diagnostically or therapeutically. Prepn. of a cDNA encoding the human thrombin receptor is described. Activity of a large variety of thrombin agonist and antagonist peptides is reported. Also reported are the prepn., using oligonucleotide-directed mutagenesis, of active-site thrombin mutants and the activity thereof, as well as prepn. and testing of (monoclonal) antibodies.

L4 ANSWER 93 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1992:470301 CAPLUS  
 DN 117:70301  
 TI Synthesis of peptides containing .alpha.,.alpha.-diphenylglycine  
 AU Yamada, Takashi; Omote, Yuichiro; Miyazawa, Toshifumi; Kuwata, Shigeru; Matsumoto, Kiyoshi  
 CS Fac. Sci., Konan Univ., Kobe, 658, Japan  
 SO Peptide Chemistry (1992), Volume Date 1991, 29th, 367-72  
 CODEN: PECHDP; ISSN: 0388-3698  
 DT Journal  
 LA English  
 OS CASREACT 117:70301  
 IT **142618-65-3P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. and hydrogenolysis of)  
 RN 142618-65-3 CAPLUS  
 CN L-Leucine, N-[N-[N-[2,2-diphenyl-N-[N-[(phenylmethoxy)carbonyl]-O-(phenylmethyl)-L-tyrosyl]glycyl]glycyl]-L-phenylalanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



—Bu-i

## IT 142618-63-1P

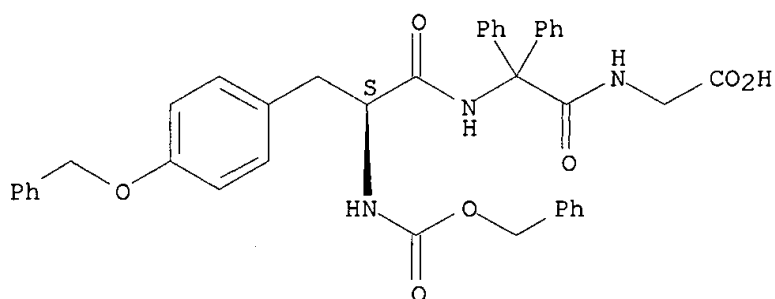
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and peptide coupling of, with dipeptide Me ester)

RN 142618-63-1 CAPLUS

CN Glycine, N-[2,2-diphenyl-N-[N-[(phenylmethoxy)carbonyl]-O-(phenylmethyl)-L-tyrosyl]glycyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



## IT 142618-64-2P

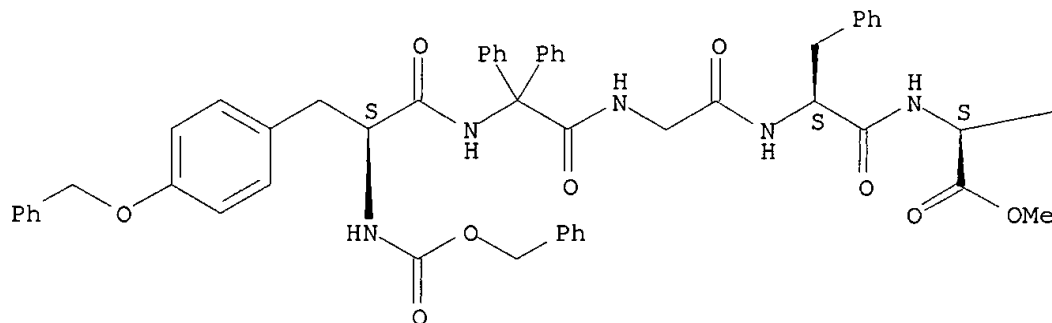
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and sapon. of)

RN 142618-64-2 CAPLUS

CN L-Leucine, N-[N-[N-[2,2-diphenyl-N-[N-[(phenylmethoxy)carbonyl]-O-(phenylmethyl)-L-tyrosyl]glycyl]glycyl]-L-phenylalanyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.





—Bu-i

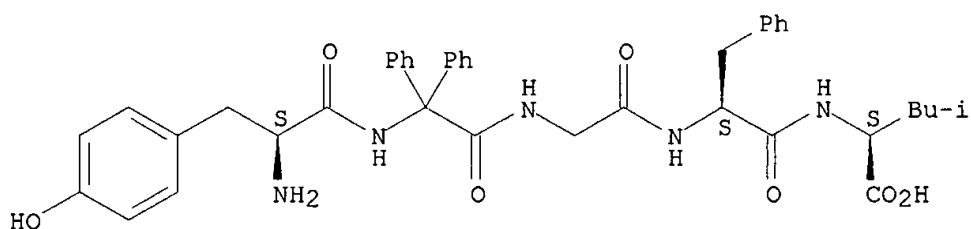
IT **142618-66-4P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 142618-66-4 CAPLUS

CN L-Leucine, N-[N-[N-(2,2-diphenyl-N-L-tyrosylglycyl)glycyl]-L-phenylalanyl]-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



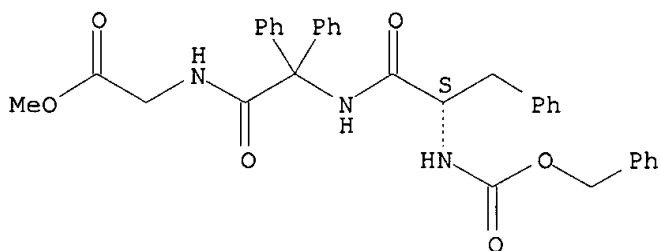
IT **142618-58-4P 142618-59-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, by Ugi reaction)

RN 142618-58-4 CAPLUS

CN Glycine, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-2,2-diphenylglycyl-,  
methyl ester (9CI) (CA INDEX NAME)

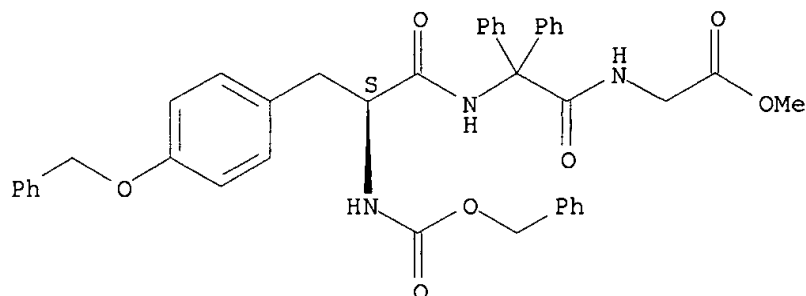
Absolute stereochemistry.



RN 142618-59-5 CAPLUS

CN Glycine, N-[2,2-diphenyl-N-[N-[(phenylmethoxy)carbonyl]-O-(phenylmethyl)-L-tyrosyl]glycyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Peptides contg. .alpha.,.alpha.-diphenylglycine (Dpg) were prepd. using the Ugi reaction. The Ugi reaction of Z-AA-OH [Z = PhCH2O2C; AA = Ala, Val, Leu, Phe, Tyr(Bzl) (Bzl = benzyl), .alpha.-aminoisobutyric acid (Aib), Ac5C, Dph] with HN:CPh2 and CNCH2CO2Me gave Z-AA-Dph-Gly-OMe. The above reactions were done at 9 kbar and 1 bar pressure; the effect of high pressure was scarcely obsd. Z-Tyr(Bzl)-Dph-Gly-OMe was used in the synthesis of enkephalin analog H-Tyr-Dph-Gly-Phe-Leu-OH. HCO-Aib-OMe was treated with diphosgene to give isocyanide CHCMe2CO2Me, which underwent the Ugi reaction with Z-AA-OH (AA = Aib, Ac3c, Ac5c, Dph) and HN:CPh2 gave Z-AA-Dph-Aib-OMe. HCO2H was treated with HN:CPh2 and CNcHex (cHex = cyclohexyl) to give HCO-Dph-NHcHex, which was treated with diphosgene to give CNCPh2CONHcHex, which was treated with Z-Dph-OH and HN:CPh2 to give Z-Dph-Dph-Dph-NHcHex.

L4 ANSWER 94 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1991:608499 CAPLUS

DN 115:208499

TI Design and synthesis of HIV protease inhibitors. Variations of the carboxyterminus of the HIV protease inhibitor L-682,679

AU DeSolms, S. Jane; Giuliani, Elizabeth A.; Guare, James P.; Vacca, Joseph P.; Sanders, William M.; Graham, Samuel L.; Wiggins, J. Mark; Darke, Paul L.; Sigal, Irving S.; et al.

CS Merck Sharp and Dohme Res. Lab., West Point, PA, 19486, USA

SO Journal of Medicinal Chemistry (1991), 34(9), 2852-7

CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

OS CASREACT 115:208499

IT **135832-68-7P 135832-70-1P 135911-86-3P**

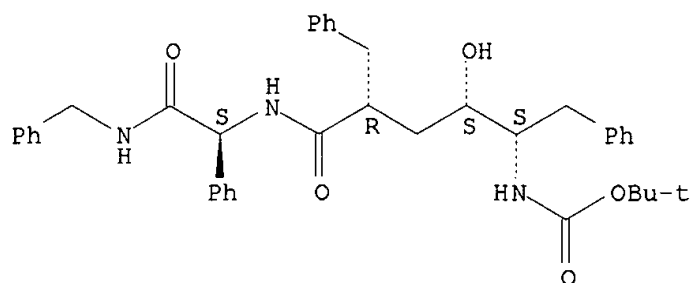
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and HIV protease-inhibiting activity of)

RN 135832-68-7 CAPLUS

CN Carbamic acid, [2-hydroxy-5-oxo-5-[[2-oxo-1-phenyl-2-[(phenylmethyl)amino]ethyl]amino]-1,4-bis(phenylmethyl)pentyl]-, 1,1-dimethylethyl ester, [1S-[1R\*,2R\*,4S\*,5(R\*)]]- (9CI) (CA INDEX NAME)

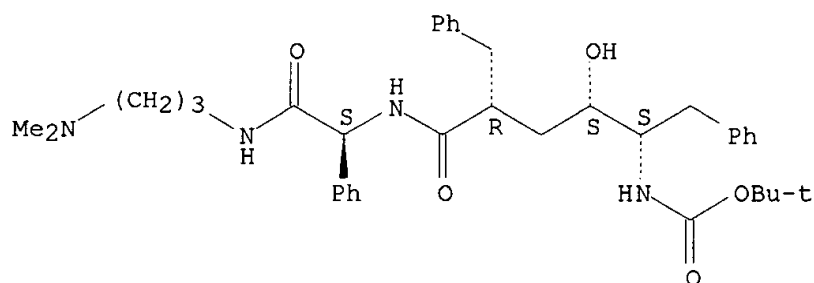
Absolute stereochemistry.



RN 135832-70-1 CAPLUS

CN 2,6,9,15-Tetraazaahexadecan-16-oic acid, 13-hydroxy-2-methyl-7,10-dioxo-8-phenyl-11,14-bis(phenylmethyl)-, 1,1-dimethylethyl ester, [8S-(8R\*,11S\*,13R\*,14R\*)]-(9CI) (CA INDEX NAME)

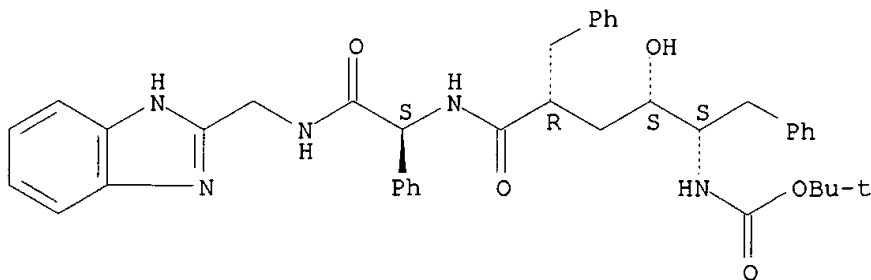
Absolute stereochemistry.



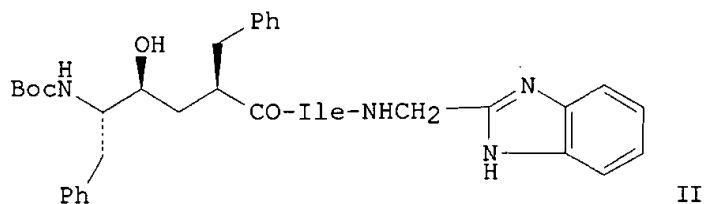
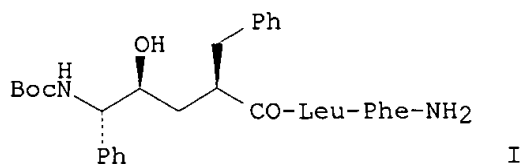
RN 135911-86-3 CAPLUS

CN Carbamic acid, [5-[[2-[(1H-benzimidazol-2-ylmethyl)amino]-2-oxo-1-phenylethyl]amino]-2-hydroxy-5-oxo-1,4-bis(phenylmethyl)pentyl]-, 1,1-dimethylethyl ester, [1S-[1R\*,2R\*,4S\*,5(R\*)]]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB L-682,679 (I, Boc = Me<sub>3</sub>CO<sub>2</sub>C) tetrapeptide analogs, in which the carboxy terminus has been shortened and modified, were prepd. and their inhibitory activity measured against the HIV protease in a peptide cleavage assay. Selected examples were tested as inhibitors of virus spread in cell culture. Analog II was a 10-fold more potent enzyme inhibitor than I in vitro and 30-fold more potent in inhibiting the viral spread in cells.

L4 ANSWER 95 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1991:508772 CAPLUS

DN 115:108772

TI Site-specific incorporation of non-natural residues into peptides: effect of residue structure on suppression and translation efficiencies

AU Bain, J. D.; Wacker, Dean A.; Kuo, Eric E.; Chamberlain, A. Richard

CS Dep. Chem., Univ. California, Irvine, CA, 92717, USA

SO Tetrahedron (1991), 47(14-15), 2389-400

CODEN: TETRAB; ISSN: 0040-4020

DT Journal

LA English

IT **135674-10-1P**

RL: SPN (Synthetic preparation); PREP (Preparation)

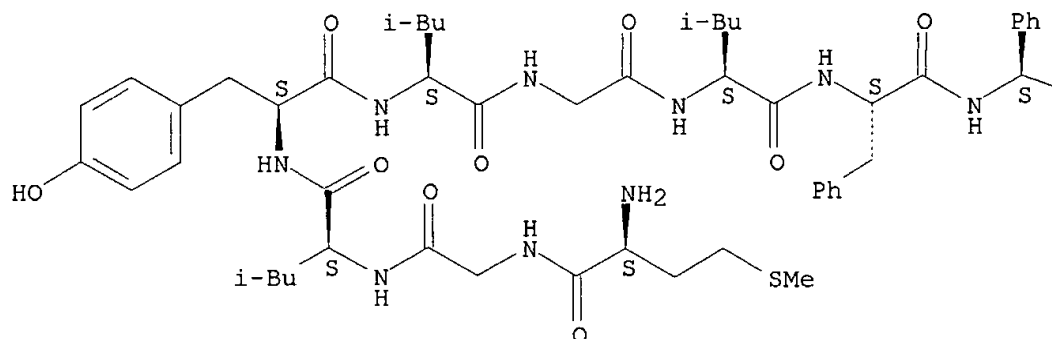
(prepn. of, by site-specific mutagenesis with unnatural acylated tRNAs, translation efficiency in)

RN 135674-10-1 CAPLUS

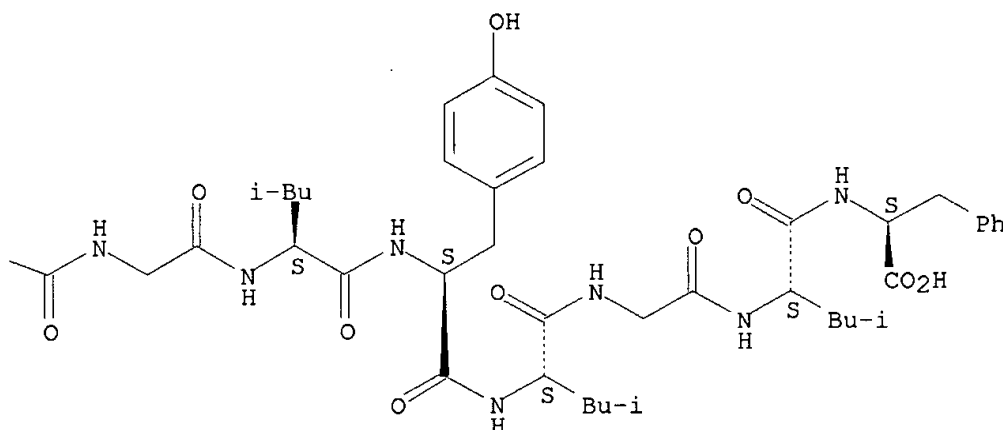
CN L-Phenylalanine, L-methionylglycyl-L-leucyl-L-tyrosyl-L-leucylglycyl-L-leucyl-L-phenylalanyl-L-2-phenylglycylglycyl-L-leucyl-L-tyrosyl-L-leucylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



AB A systematic survey of the structural requirements for biosynthetic incorporation of nonnatural residues into a polypeptide is presented. Relative translation efficiencies for a series of 12 semisynthetic acylated suppressor tRNAs ranged from 0 to 91%, depending on the structure of the residue incorporated.

L4 ANSWER 96 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1991:49567 CAPLUS

DN 114:49567

TI Dihydropyridine derivative redox systems for brain-targeted drug delivery

IN Bodor, Nicholas S.

PA University of Florida, USA

SO Eur. Pat. Appl., 120 pp.

CODEN: EPXXDW

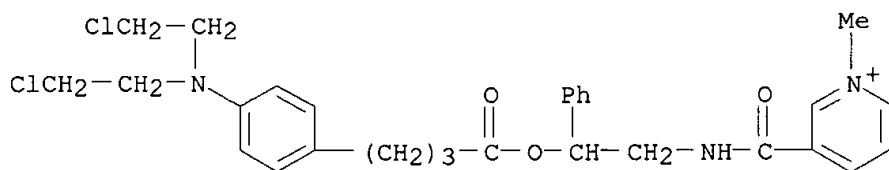
DT Patent

LA English  
FAN.CNT 2

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.   | DATE     |
|----|---|------|----------|-------------------|----------|
| PI | EP 327766   | A2   | 19890816 | EP 1988-312016    | 19881219 |
|    | EP 327766   | A3   | 19900926 |                   |          |
|    | EP 327766   | B1   | 19980408 |                   |          |
|    | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                   |          |
|    | US 5002935  | A    | 19910326 | US 1987-139755 A  | 19871230 |
|    | CA 1331564  | A1   | 19940823 | US 1987-139755    | 19871230 |
|    |   |      |          | CA 1988-585791    | 19881213 |
|    | AT 164855   | E    | 19980415 | US 1987-139755 A  | 19871230 |
|    |   |      |          | AT 1988-312016    | 19881219 |
|    | ES 2118707  | T3   | 19981001 | US 1987-139755 A  | 19871230 |
|    |   |      |          | ES 1988-312016    | 19881219 |
|    | AU 8827339  | A1   | 19890706 | US 1987-139755 A  | 19871230 |
|    | AU 619788   | B2   | 19920206 | AU 1988-27339     | 19881221 |
|    |   |      |          | US 1987-139755 A  | 19871230 |
|    | ZA 8809679  | A    | 19900829 | ZA 1988-9679      | 19881228 |
|    |   |      |          | US 1987-139755 A  | 19871230 |
|    | JP 01294663   | A2   | 19891128 | JP 1989-37        | 19890104 |
|    | JP 3038715  | B2   | 20000508 |                   |          |
|    |   |      |          | US 1987-139755 A  | 19871230 |
|    | EP 335545   | A2   | 19891004 | EP 1989-302719    | 19890320 |
|    | EP 335545   | A3   | 19900926 |                   |          |
|    | EP 335545   | B1   | 19930609 |                   |          |
|    | EP 335545   | B2   | 19980923 |                   |          |
|    | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                   |          |
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|    | AT 90200  | E    | 19930615 | EP 1988-312016 A  | 19881219 |
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|    | ES 2058503  | T3   | 19941101 | EP 1989-302719 A  | 19890320 |
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|    | AU 8931762  | A1   | 19890727 | EP 1988-312016 A  | 19881219 |
|    | AU 618995   | B2   | 19920116 | AU 1989-31762     | 19890328 |
|    |   |      |          | US 1987-139755 A  | 19871230 |
|    |   |      |          | US 1988-174945 A  | 19880329 |
|    | US 5017566  | A    | 19910521 | US 1989-431222    | 19891103 |
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|    |   |      |          | US 1988-174945 A2 | 19880329 |
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|    |   |      |          | IE 1988-3717 A    | 19881213 |
|    |   |      |          | IE 1989-810 A     | 19890314 |
|    | US 5024998  | A    | 19910618 | US 1989-448655    | 19891211 |
|    |   |      |          | US 1987-139755 A2 | 19871230 |
|    |   |      |          | US 1988-174945 A2 | 19880329 |
|    |   |      |          | CA 1988-585791 A  | 19881213 |
|    |   |      |          | IE 1988-3717 A    | 19881213 |
|    |   |      |          | IE 1989-810 A     | 19890314 |
|    |   |      |          | US 1989-431222 A2 | 19891103 |

PATENT FAMILY INFORMATION:  
FAN 1990:446267

|     | PATENT NO.   | KIND | DATE     | APPLICATION NO.   | DATE     |
|-----|--|------|----------|-------------------|----------|
| PI  | EP 335545  | A2   | 19891004 | EP 1989-302719    | 19890320 |
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|     | EP 335545  | B1   | 19930609 |                   |          |
|     | EP 335545  | B2   | 19980923 |                   |          |
|     | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE  |      |          |                   |          |
|     |  |      |          | US 1988-174945 A  | 19880329 |
|     |  |      |          | EP 1988-312016 A  | 19881219 |
|     | US 4983586   | A    | 19910108 | US 1988-174945    | 19880329 |
|     |  |      |          | US 1987-139755 A2 | 19871230 |
|     | EP 327766  | A2   | 19890816 | EP 1988-312016    | 19881219 |
|     | EP 327766  | A3   | 19900926 |                   |          |
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|     | AU 8931762   | A1   | 19890727 | AU 1989-31762     | 19890328 |
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|     |  |      |          | US 1987-139755 A  | 19871230 |
|     |  |      |          | US 1988-174945 A  | 19880329 |
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|     |  |      |          | US 1988-174945 A  | 19880329 |
|     | JP 02009825  | A2   | 19900112 | JP 1989-77938     | 19890329 |
|     | JP 2643426   | B2   | 19970820 |                   |          |
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|     | ZA 8902315   | A    | 19901228 | ZA 1989-2315      | 19890329 |
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|     | US 5017566   | A    | 19910521 | US 1989-431222    | 19891103 |
|     |  |      |          | US 1987-139755 A2 | 19871230 |
|     |  |      |          | US 1988-174945 A2 | 19880329 |
|     |  |      |          | CA 1988-585791 A  | 19881213 |
|     |  |      |          | IE 1988-3717 A    | 19881213 |
|     |  |      |          | IE 1989-810 A     | 19890314 |
|     | US 5024998   | A    | 19910618 | US 1989-448655    | 19891211 |
|     |  |      |          | US 1987-139755 A2 | 19871230 |
|     |  |      |          | US 1988-174945 A2 | 19880329 |
|     |  |      |          | CA 1988-585791 A  | 19881213 |
|     |  |      |          | IE 1988-3717 A    | 19881213 |
|     |  |      |          | IE 1989-810 A     | 19890314 |
|     |  |      |          | US 1989-431222 A2 | 19891103 |
| IT  | <b>123630-90-0P 123630-97-7P</b>   |      |          |                   |          |
|     | RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  |      |          |                   |          |
|     | (prepn. and reaction of, in drug delivery system prepn.)   |      |          |                   |          |
| RN  | 123630-90-0 CAPLUS   |      |          |                   |          |
| CN  | Pyridinium, 3-[[[2-[4-[4-[bis(2-chloroethyl)amino]phenyl]-1-oxobutoxy]-2-phenylethyl]amino]carbonyl]-1-methyl-, methyl sulfate (9CI) (CA INDEX NAME) |      |          |                   |          |
| CM  | 1  |      |          |                   |          |
| CRN | 123630-89-7  |      |          |                   |          |
| CMF | C29 H34 Cl2 N3 O3  |      |          |                   |          |



CM 2

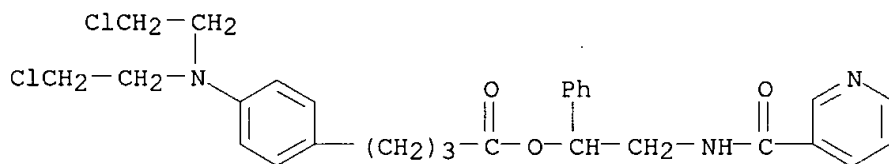
CRN 21228-90-0

CMF C H3 O4 S

Me-O-SO<sub>3</sub><sup>-</sup>

RN 123630-97-7 CAPLUS

CN Benzenebutanoic acid, 4-[bis(2-chloroethyl)amino]-, 1-phenyl-2-[(3-pyridinylcarbonyl)amino]ethyl ester (9CI) (CA INDEX NAME)

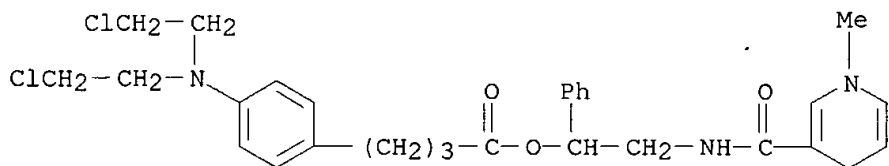
IT **123630-82-0DP**, inclusion complexes with cyclodextrin derivs.

RL: PREP (Preparation)

(prepn. of, for brain targeting)

RN 123630-82-0 CAPLUS

CN Benzenebutanoic acid, 4-[bis(2-chloroethyl)amino]-, 2-[[[1,4-dihydro-1-methyl-3-pyridinyl)carbonyl]amino]-1-phenylethyl ester (9CI) (CA INDEX NAME)



AB Inclusion complexes of hydroxypropyl, hydroxyethyl, glucosyl, maltosyl or maltotriosyl derivs. of .beta.- or .gamma.- cyclodextrin with the reduced, biooxidizable, blood-brain barrier penetrating, lipoidal forms of dihydropyridine pyridinium salt redox systems for brain-targeted drug delivery provide a means for stabilizing the redox systems, particularly against oxidn. The redox inclusion complexes also provide a means for decreasing initial drug concns. in the lungs after administration of the



systems, leading to decreased toxicity. In selected instances, complexation results in substantially improved water soly. of the redox systems as well. The dihydropyridine lipidal forms are e.g. 1-methyl-3-[[N-.beta.-[3,4-bis(pivalyloxy)phenyl]ethylcarbamoyl]]-1,4-dihydropyridine and 3-hydroxy-17.beta.-[(methyl-1,4-dihydropyridin-3-yl)carbonyl]oxyetra-1,3,5(10)-triene (E2-CDS). Thus, the soly. of E2-CDS-2-hydroxypropyl .beta. -cyclodextrin complexes was .apprx.30 mg/mL vs. 0.0002 mg/mL for E2-CDS. In Sprague-Dawley rats, the lung level of a quaternary ammonium salt after i.v. administration of the complex was lower than that after i.v. administration of E2CDS.

L4 ANSWER 97 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1990:446267 CAPLUS  
 DN 113:46267  
 TI Pharmaceutical formulations for parenteral use containing cyclodextrins and dihydropyridine redox systems  
 IN Bodor, Nicholas S.  
 PA University of Florida, USA  
 SO Eur. Pat. Appl., 125 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 2

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.   | DATE     |
|----|---|------|----------|-------------------|----------|
| PI | EP 335545   | A2   | 19891004 | EP 1989-302719    | 19890320 |
|    | EP 335545   | A3   | 19900926 |                   |          |
|    | EP 335545   | B1   | 19930609 |                   |          |
|    | EP 335545   | B2   | 19980923 |                   |          |
|    | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                   |          |
|    |   |      |          | US 1988-174945 A  | 19880329 |
|    |   |      |          | EP 1988-312016 A  | 19881219 |
|    | US 4983586  | A    | 19910108 | US 1988-174945    | 19880329 |
|    |   |      |          | US 1987-139755 A2 | 19871230 |
|    | EP 327766   | A2   | 19890816 | EP 1988-312016    | 19881219 |
|    | EP 327766   | A3   | 19900926 |                   |          |
|    | EP 327766   | B1   | 19980408 |                   |          |
|    | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                   |          |
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|    |   |      |          | US 1988-174945 A  | 19880329 |
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|    | AU 8931762  | A1   | 19890727 | AU 1989-31762     | 19890328 |
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|    |   |      |          | US 1988-174945 A  | 19880329 |
|    | CA 1336498  | A1   | 19950801 | CA 1989-594911    | 19890328 |
|    |   |      |          | US 1988-174945 A  | 19880329 |
|    | JP 02009825   | A2   | 19900112 | JP 1989-77938     | 19890329 |
|    | JP 2643426  | B2   | 19970820 |                   |          |
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|    |   |      |          | US 1988-174945 A  | 19880329 |
|    | US 5017566  | A    | 19910521 | US 1989-431222    | 19891103 |
|    |   |      |          | US 1987-139755 A2 | 19871230 |
|    |   |      |          | US 1988-174945 A2 | 19880329 |

US 5024998 A 19910618

CA 1988-585791 A 19881213  
 IE 1988-3717 A 19881213  
 IE 1989-810 A 19890314  
 US 1989-448655 19891211  
 US 1987-139755 A219871230  
 US 1988-174945 A219880329  
 CA 1988-585791 A 19881213  
 IE 1988-3717 A 19881213  
 IE 1989-810 A 19890314  
 US 1989-431222 A219891103

PATENT FAMILY INFORMATION:

FAN 1991:49567

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO.           | DATE     |
|----|---|------|----------|---------------------------|----------|
| PI | EP 327766   | A2   | 19890816 | EP 1988-312016            | 19881219 |
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|    | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                           |          |
|    | US 5002935  | A    | 19910326 | US 1987-139755 A          | 19871230 |
|    | CA 1331564  | A1   | 19940823 | US 1987-139755            | 19871230 |
|    |   |      |          | CA 1988-585791            | 19881213 |
|    |   |      |          | US 1987-139755 A          | 19871230 |
|    | AT 164855   | E    | 19980415 | AT 1988-312016            | 19881219 |
|    |   |      |          | US 1987-139755 A          | 19871230 |
|    | ES 2118707  | T3   | 19981001 | ES 1988-312016            | 19881219 |
|    |   |      |          | US 1987-139755 A          | 19871230 |
|    | AU 8827339  | A1   | 19890706 | AU 1988-27339             | 19881221 |
|    | AU 619788   | B2   | 19920206 |                           |          |
|    |   |      |          | US 1987-139755 A          | 19871230 |
|    | ZA 8809679  | A    | 19900829 | ZA 1988-9679              | 19881228 |
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|    | JP 01294663   | A2   | 19891128 | JP 1989-37                | 19890104 |
|    | JP 3038715  | B2   | 20000508 |                           |          |
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|    | EP 335545   | B2   | 19980923 |                           |          |
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|    | ES 2058503  | T3   | 19941101 | ES 1989-302719            | 19890320 |
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|    | AU 8931762  | A1   | 19890727 | AU 1989-31762             | 19890328 |
|    | AU 618995   | B2   | 19920116 |                           |          |
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|    | US 5017566  | A    | 19910521 | US 1989-431222            | 19891103 |
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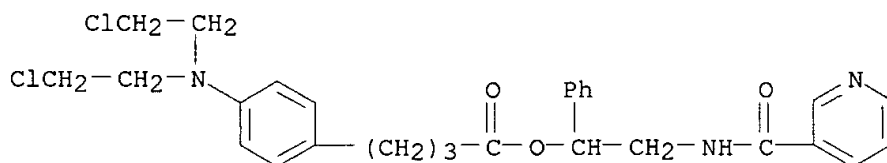
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| US 5024998 | A | 19910618 | IE 1989-810    | A 19890314 |
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|            |   |          | US 1987-139755 | A219871230 |
|            |   |          | US 1988-174945 | A219880329 |
|            |   |          | CA 1988-585791 | A 19881213 |
|            |   |          | IE 1988-3717   | A 19881213 |
|            |   |          | IE 1989-810    | A 19890314 |
|            |   |          | US 1989-431222 | A219891103 |

## IT 123630-97-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and quaternization of)

RN 123630-97-7 CAPLUS

CN Benzenebutanoic acid, 4-[bis(2-chloroethyl)amino]-, 1-phenyl-2-[(3-pyridinylcarbonyl)amino]ethyl ester (9CI) (CA INDEX NAME)



## IT 123630-90-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and redn. of)

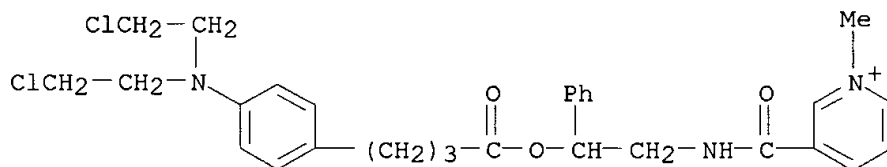
RN 123630-90-0 CAPLUS

CN Pyridinium, 3-[[[2-[4-[4-[bis(2-chloroethyl)amino]phenyl]-1-oxobutoxy]-2-phenylethyl]amino]carbonyl]-1-methyl-, methyl sulfate (9CI) (CA INDEX NAME)

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CRN 123630-89-7

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CM 2

CRN 21228-90-0

CMF C H3 O4 S

Me-O-SO3<sup>-</sup>

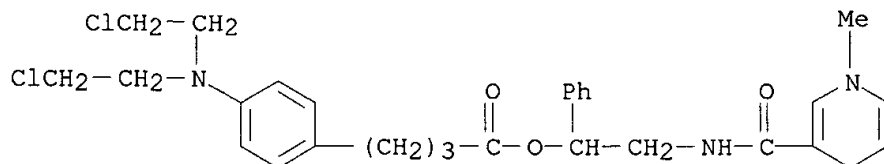
IT 123630-82-0P

RL: PREP (Preparation)

(prepn. of, for redox parenteral drug delivery systems)

RN 123630-82-0 CAPLUS

CN Benzenebutanoic acid, 4-[bis(2-chloroethyl)amino]-, 2-[[[(1,4-dihydro-1-methyl-3-pyridinyl)carbonyl]amino]-1-phenylethyl ester (9CI) (CA INDEX NAME)



AB Aq. parenteral solns. of drugs which are insol. or only sparingly sol. and/or which are unstable in water, are combined with a cyclodextrin deriv. to provide a means for alleviating problems assocd. with drug pptn. at the injection site and/or in the lungs or other organs following parenteral administration. Another approach is use of the dihydropyridine-pyridinium redox delivery system. A large no. of examples are given for synthesis of dihydropyridine and pyridinium derivs. of drugs. Data are also presented showing drug solubilization by cyclodextrin derivs.

L4 ANSWER 98 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1990:217522 CAPLUS

DN 112:217522

TI Improved solid-phase synthesis of luteinizing hormone releasing hormone analogs using 9-fluorenylmethoxycarbonyl amino acid active esters and catalytic transfer hydrogenation with minimal side-chain protection and their biological activities

AU Sivanandaiah, K. M.; Gurusiddappa, S.; Gowda, D. Channe; Babu, V. V. Suresh

CS Cent. Coll., Bangalore Univ., Bangalore, 560 001, India

SO Journal of Biosciences (Bangalore, India) (1989), 14(3), 311-17

CODEN: JOBSDN; ISSN: 0250-5991

DT Journal

LA English

IT 126706-24-9P 126706-26-1P 126706-29-4P

126733-80-0P 126733-81-1P

RL: SPN (Synthetic preparation); PREP (Preparation)

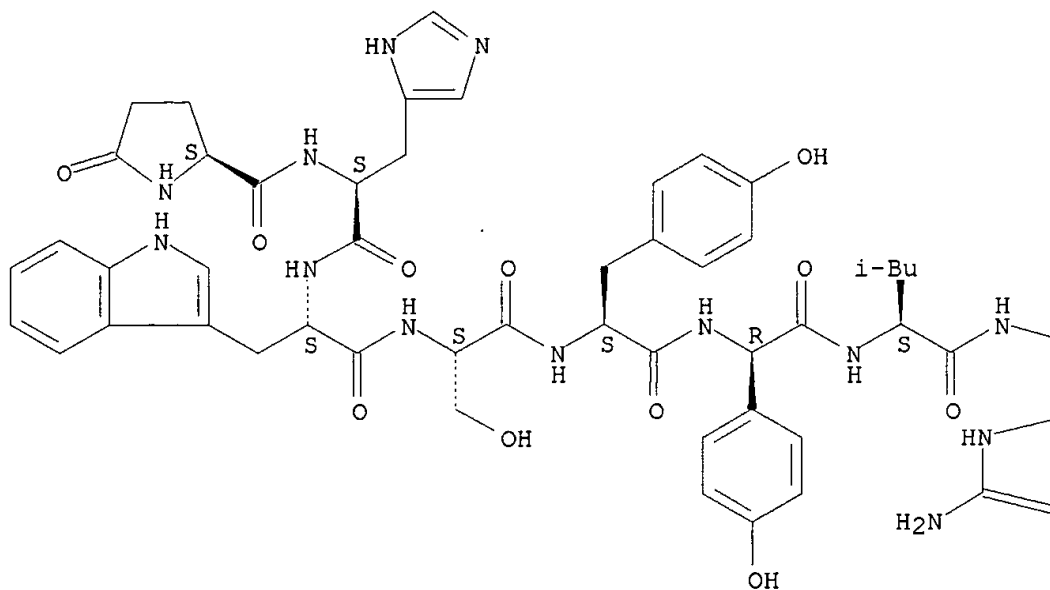
(prepn. and LH-releasing activity of)

RN 126706-24-9 CAPLUS

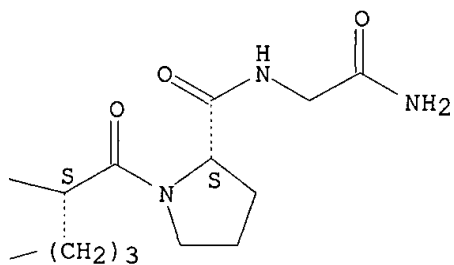
CN Luteinizing hormone-releasing factor (swine), 6-[D-2-(4-hydroxyphenyl)glycine]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



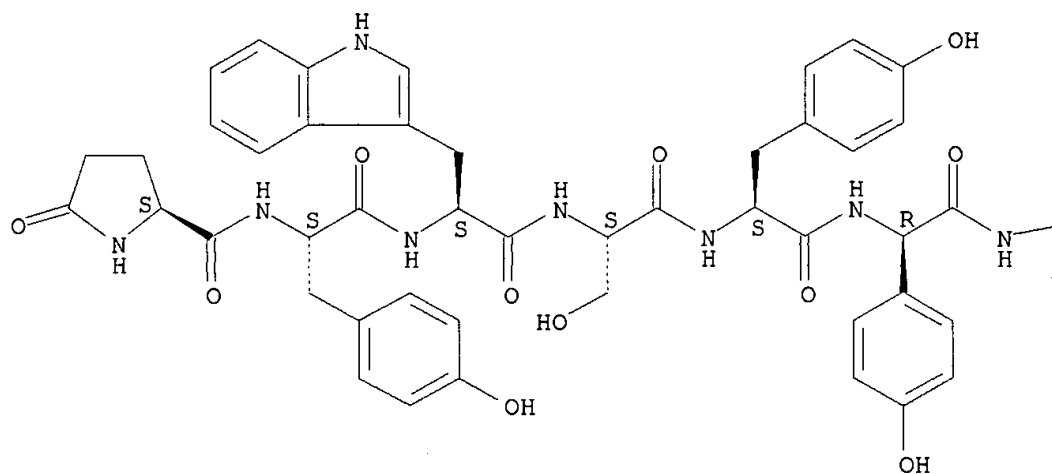
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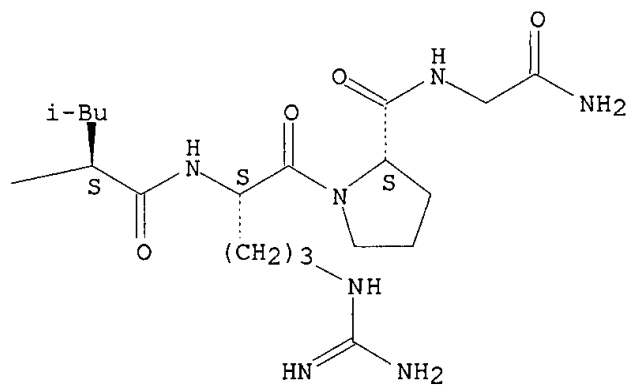
CN Luteinizing hormone-releasing factor (swine), 2-L-tyrosine-6-[D-2-(4-hydroxyphenyl)glycine]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

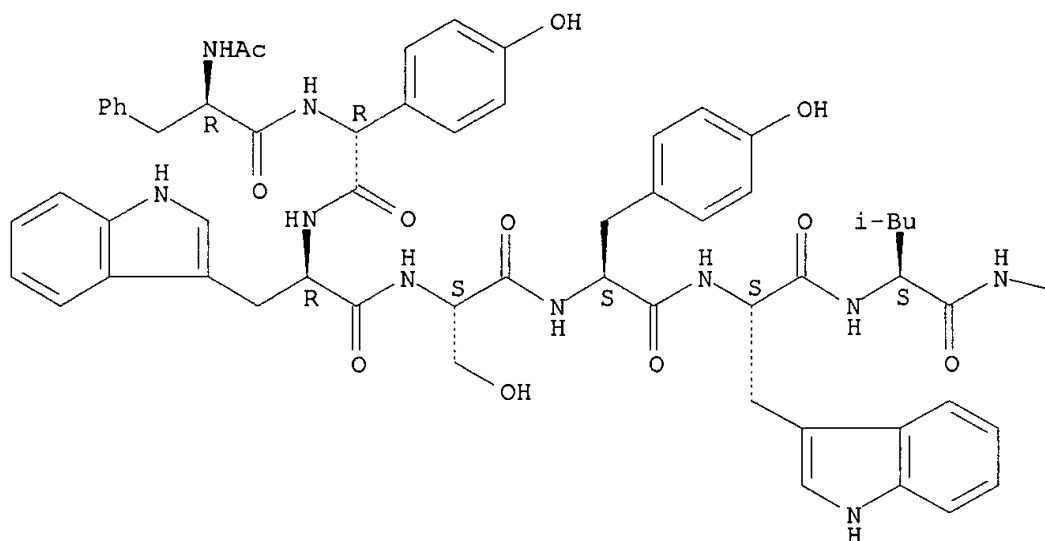


RN 126706-29-4 CAPLUS

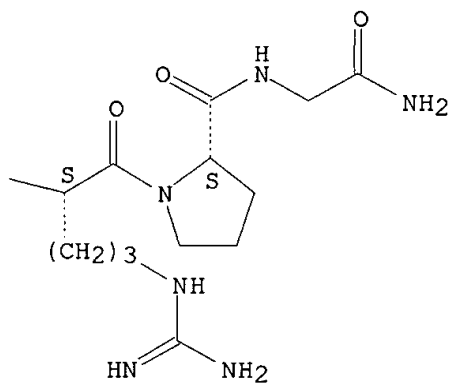
CN Luteinizing hormone-releasing factor (swine), 1-(N-acetyl-D-phenylalanine)-  
2-[D-2-(4-hydroxyphenyl)glycine]-3-D-tryptophan-6-L-tryptophan- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

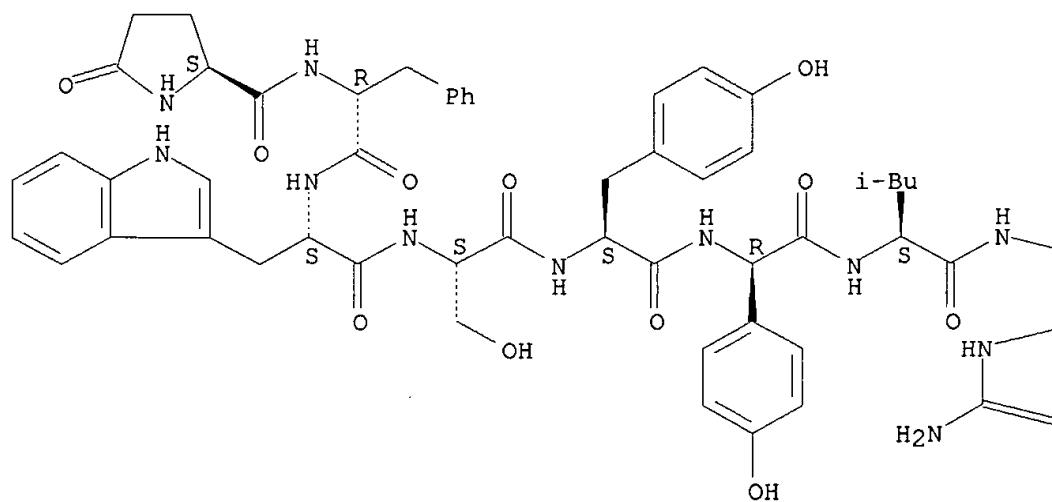


RN 126733-80-0 CAPLUS

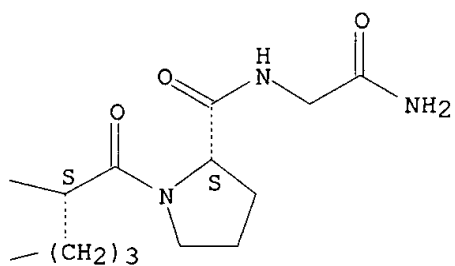
CN Luteinizing hormone-releasing factor (swine), 2-D-phenylalanine-6-[D-2-(4-hydroxyphenyl)glycine]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



=NH

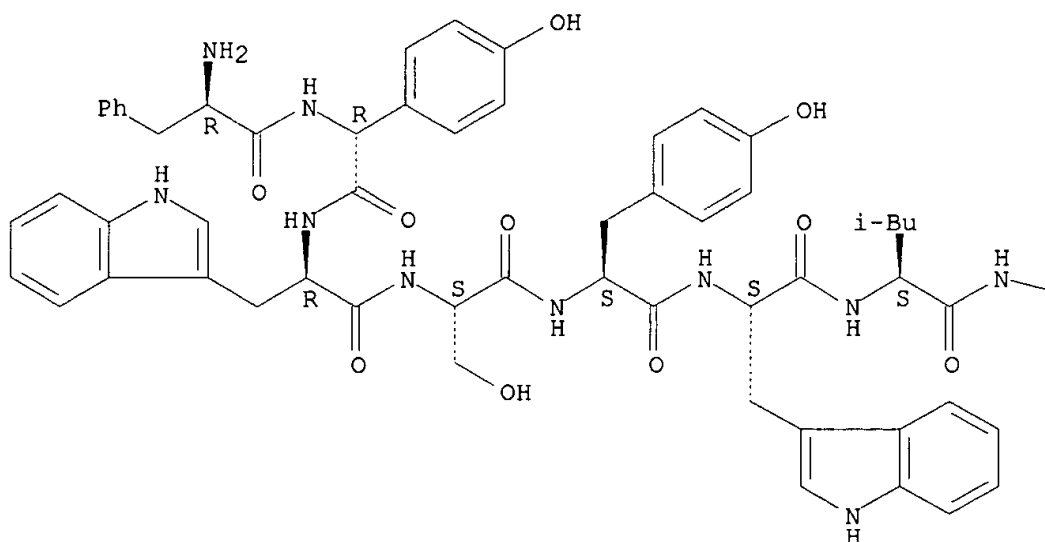
RN 126733-81-1 CAPLUS

CN Luteinizing hormone-releasing factor (swine), 1-D-phenylalanine-2-[D-2-(4-hydroxyphenyl)glycine]-3-D-tryptophan-6-L-tryptophan- (9CI) (CA INDEX NAME)

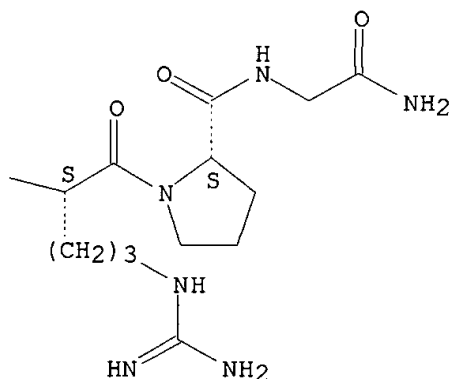
Absolute stereochemistry.



PAGE 1-A



PAGE 1-B



IT 126733-86-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

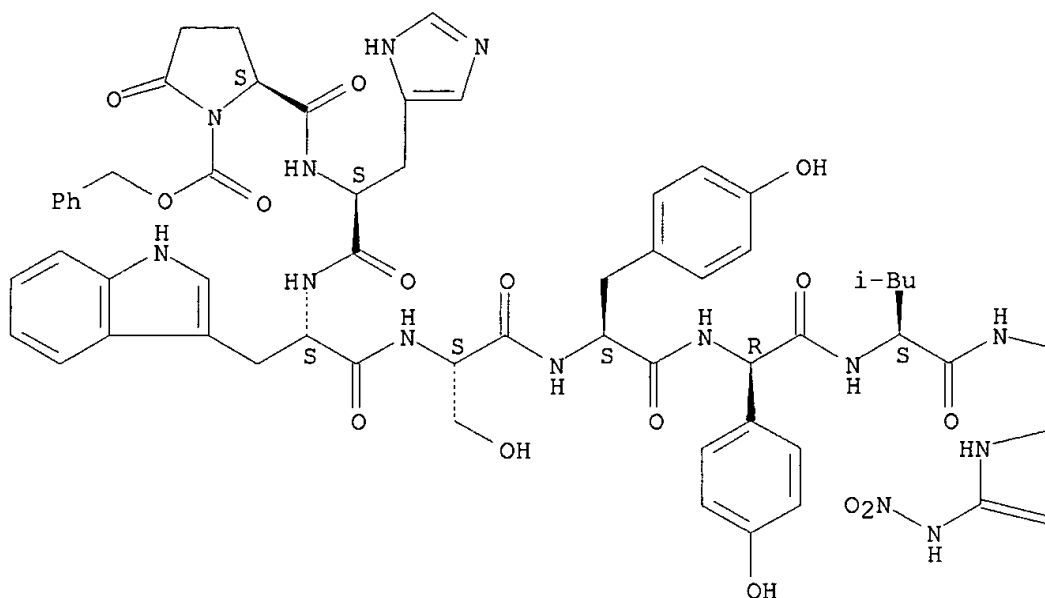
(prepn. and catalytic transfer hydrogenolysis of)

RN 126733-86-6 CAPLUS

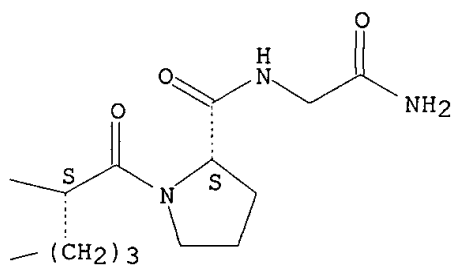
CN Luteinizing hormone-releasing factor (swine), 1-[5-oxo-1-[(phenylmethoxy)carbonyl]-L-proline]-6-[D-2-(4-hydroxyphenyl)glycine]-8-[N5-[imino(nitroamino)methyl]-L-ornithine]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

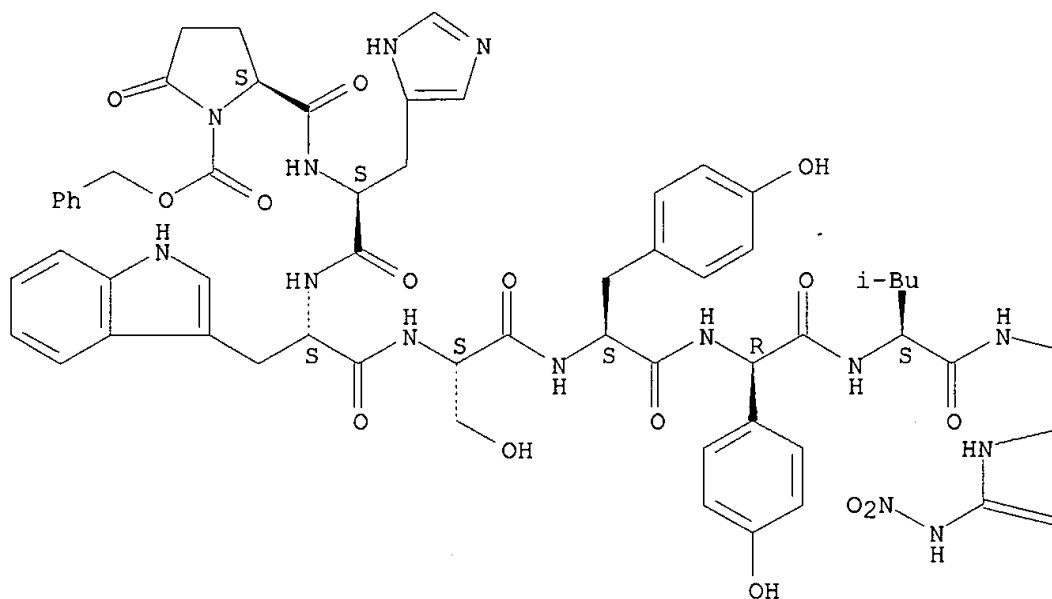


=NH

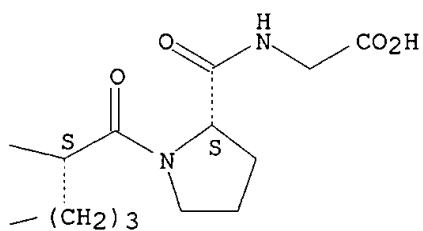
IT **126706-32-9DP**, ester with benzyloxybenzyl alc. resin  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and resin cleavage of, by ammonolysis)  
 RN 126706-32-9 CAPLUS  
 CN Luteinizing hormone-releasing factor (swine), 1-[5-oxo-1-  
 [(phenylmethoxy)carbonyl]-L-proline]-6-[D-2-(4-hydroxyphenyl)glycine]-8-  
 [N5-[imino(nitroamino)methyl]-L-ornithine]-10-glycine- (9CI) (CA INDEX  
 NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



=NH

IT 127146-47-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 127146-47-8 CAPLUS

CN Luteinizing hormone-releasing factor (swine), 6-[D-2-(4-

hydroxyphenyl)glycine]-, triacetate (salt) (9CI) (CA INDEX NAME)

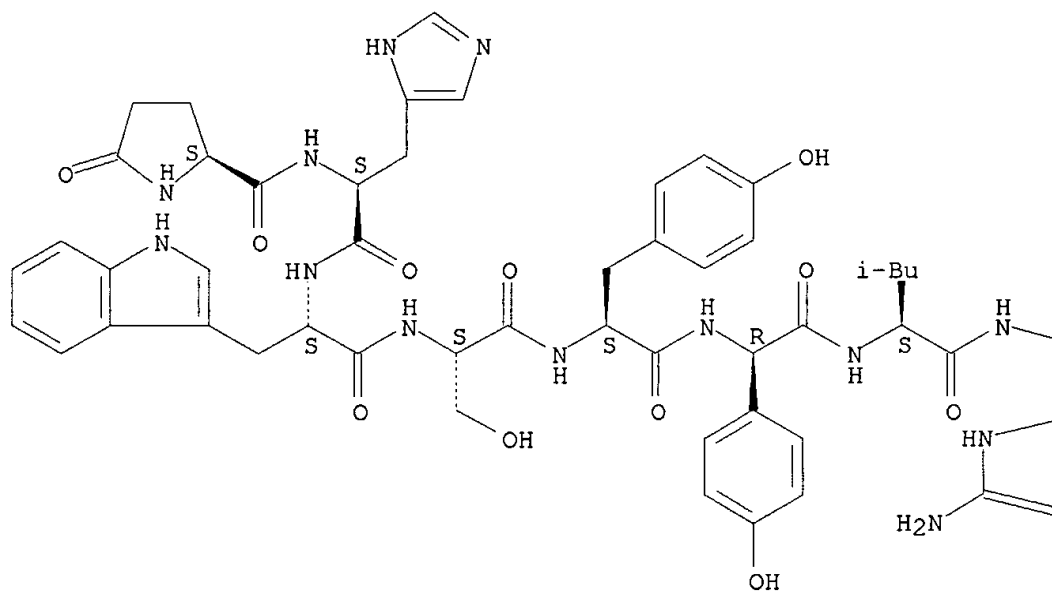
CM 1

CRN 126706-24-9

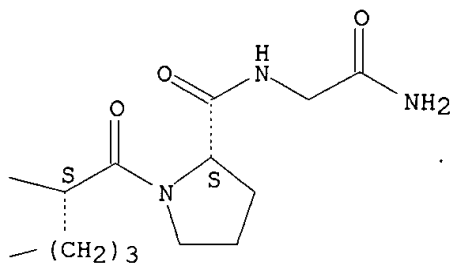
CMF C61 H79 N17 O14

Absolute stereochemistry.

PAGE 1-A

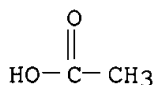


PAGE 1-B



=NH

CM 2

CRN 64-19-7  
CMF C2 H4 O2

AB Using mainly 9-fluorenylmethoxycarbonyl amino acid 2,4,5-trichlorophenyl esters in the presence of 1-hydroxybenzotriazole and the solid support p-alkoxybenzyl alc. resin, synthesis of LH releasing hormone analogs was carried out with minimal side-chain protection. Catalytic transfer hydrogenation was employed for removal of NO<sub>2</sub> and Z-groups from Arg and pyroglutamic acid, resp., avoiding the use of HF; this led to good yields. An arom., hydrophilic amino acid, D-(p-hydroxyphenyl)glycine was incorporated into LH releasing hormone mol. along with other modifications. The agonistic as well as antagonistic activities of all the peptides were studied.

L4 ANSWER 99 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1990:199132 CAPLUS

DN 112:199132

TI Preparation of human immunodeficiency virus (HIV) protease inhibitors for treatment of AIDS

IN Sigal, Irving S.; Huff, Joel R.; Darke, Paul L.; Vacca, Joseph P.; Young, Steven D.; Desolms, S. Jane; Thompson, Wayne J.; Lyle, Terry A.; Graham, Samuel L.; Ghosh, Arun K.

PA Merck and Co., Inc., USA

SO Eur. Pat. Appl., 94 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 337714   | A2   | 19891018 | EP 1989-303539  | 19890411 |
|    | EP 337714   | A3   | 19910807 |                 |          |
|    | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                 |          |
|    |   |      |          | US 1988-180507  | 19880412 |
|    |   |      |          | US 1988-236084  | 19880824 |
|    |   |      |          | US 1989-328643  | 19890328 |
|    | FI 8901716  | A    | 19891013 | FI 1989-1716    | 19890411 |
|    |   |      |          | US 1988-180507  | 19880412 |
|    |   |      |          | US 1988-236084  | 19880824 |
|    |   |      |          | US 1989-328643  | 19890328 |
|    | NO 8901489  | A    | 19891013 | NO 1989-1489    | 19890411 |
|    |   |      |          | US 1988-180507  | 19880412 |
|    |   |      |          | US 1988-236084  | 19880824 |
|    |   |      |          | US 1989-328643  | 19890328 |
|    | ZA 8902627  | A    | 19891129 | ZA 1989-2627    | 19890411 |
|    |   |      |          | US 1988-180507  | 19880412 |
|    | DK 8901723  | A    | 19891211 | DK 1989-1723    | 19890411 |
|    |   |      |          | US 1988-180507  | 19880412 |

|             |    |          |                |          |
|-------------|----|----------|----------------|----------|
|             |    |          | US 1988-236084 | 19880824 |
|             |    |          | US 1989-328643 | 19890328 |
| AU 8932706  | A1 | 19891019 | AU 1989-32706  | 19890412 |
| AU 620084   | B2 | 19920213 |                |          |
|             |    |          | US 1988-180507 | 19880412 |
|             |    |          | US 1988-236084 | 19880824 |
|             |    |          | US 1989-328643 | 19890328 |
| JP 02209854 | A2 | 19900821 | JP 1989-92762  | 19890412 |
|             |    |          | US 1988-180507 | 19880412 |
|             |    |          | US 1988-236084 | 19880824 |
|             |    |          | US 1989-328643 | 19890328 |

OS MARPAT 112:199132

IT 126409-55-0P 126409-69-6P 126409-80-1P

126409-84-5P 126409-99-2P 126410-16-0P

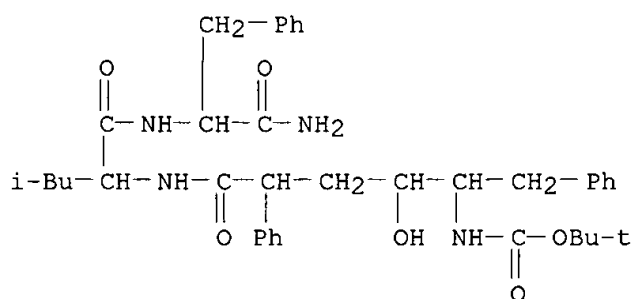
126438-28-6P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, as HIV protease inhibitor for AIDS treatment)

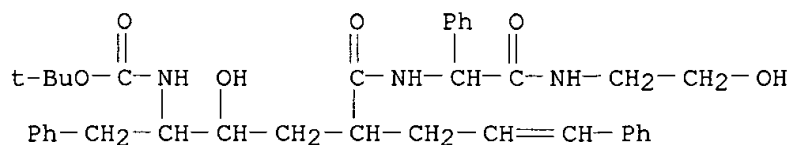
RN 126409-55-0 CAPLUS

CN L-Phenylalaninamide, N-[5-[[[(1,1-dimethylethoxy)carbonyl]amino]-4-hydroxy-1-oxo-2,6-diphenylhexyl]-L-leucyl-, [2R-(2R\*,4S\*,5S\*)]- (9CI) (CA INDEX NAME)



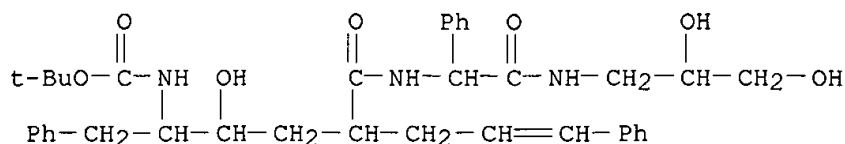
RN 126409-69-6 CAPLUS

CN Carbamic acid, [2-hydroxy-4-[[[2-[(2-hydroxyethyl)amino]-2-oxo-1-phenylethyl]amino]carbonyl]-7-phenyl-1-(phenylmethyl)-6-heptenyl]-, 1,1-dimethylethyl ester, [1S-[1R\*,2R\*,4S\*(R\*)]]- (9CI) (CA INDEX NAME)



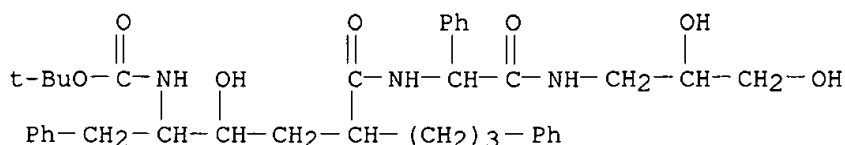
RN 126409-80-1 CAPLUS

CN Carbamic acid, [5-[[2-[(2,3-dihydroxypropyl)amino]-2-oxo-1-phenylethyl]amino]-2-hydroxy-5-oxo-1-(phenylmethyl)-4-(3-phenyl-2-propenyl)pentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



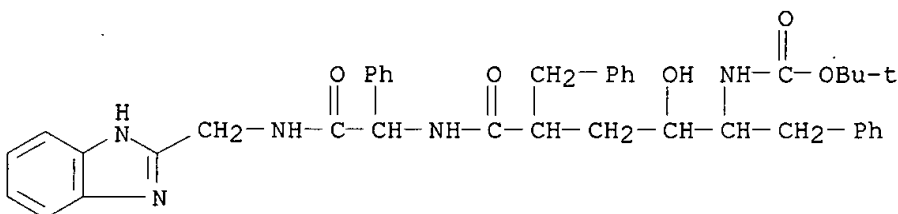
RN 126409-84-5 CAPLUS

CN Carbamic acid, [4-[[[2-[(2,3-dihydroxypropyl)amino]-2-oxo-1-phenylethyl]amino]carbonyl]-2-hydroxy-7-phenyl-1-(phenylmethyl)heptyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



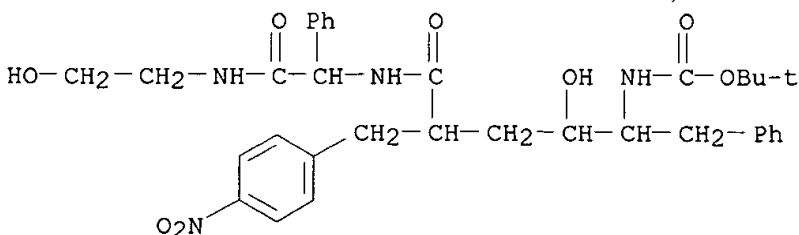
RN 126409-99-2 CAPLUS

CN Carbamic acid, [5-[[2-[(1H-benzimidazol-2-ylmethyl)amino]-2-oxo-1-phenylethyl]amino]-2-hydroxy-5-oxo-1,4-bis(phenylmethyl)pentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



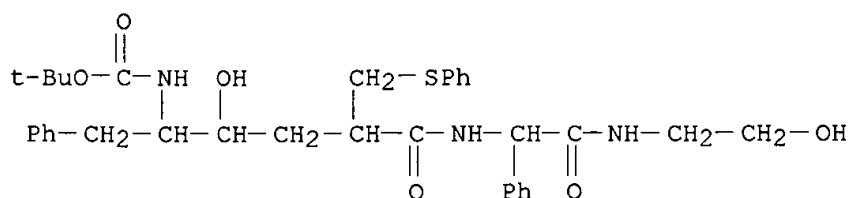
RN 126410-16-0 CAPLUS

CN Carbamic acid, [2-hydroxy-5-[[2-[(2-hydroxyethyl)amino]-2-oxo-1-phenylethyl]amino]-4-[(4-nitrophenyl)methyl]-5-oxo-1-(phenylmethyl)pentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 126438-28-6 CAPLUS

CN Carbamic acid, [2-hydroxy-5-[[2-[(2-hydroxyethyl)amino]-2-oxo-1-phenylethyl]amino]-5-oxo-1-(phenylmethyl)-4-[(phenylthio)methyl]pentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

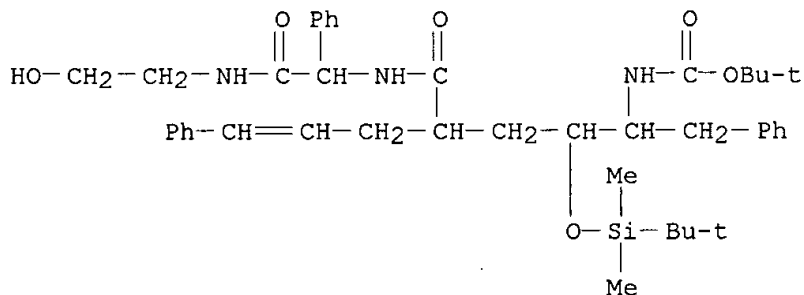


IT 126410-96-6P 126411-01-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as intermediate for HIV protease inhibitor)

RN 126410-96-6 CAPLUS

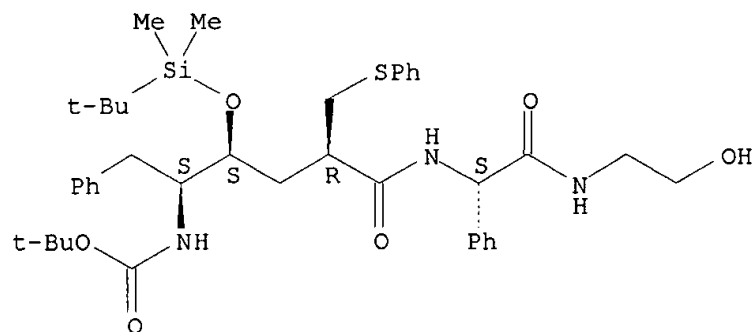
CN Carbamic acid, [2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-[[[2-[(2-hydroxyethyl)amino]-2-oxo-1-phenylethyl]amino]carbonyl]-7-phenyl-1-(phenylmethyl)-6-heptenyl]-, 1,1-dimethylethyl ester, [1S-[1R\*,2R\*,4S\*(R\*)]]- (9CI) (CA INDEX NAME)



RN 126411-01-6 CAPLUS

CN Carbamic acid, [2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-[[2-[(2-hydroxyethyl)amino]-2-oxo-1-phenylethyl]amino]-5-oxo-1-(phenylmethyl)-4-[(phenylthio)methyl]pentyl]-, 1,1-dimethylethyl ester, [1S-[1R\*,2R\*,4S\*,5(R\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI For diagram(s), see printed CA Issue.

AB Dipeptides or amino acid amides or carboxamides A-G-B-B-J [I; A = Ph3C, H, CHO, (un)substituted C2-5 alkanoyl, phthaloyl, MeO2C, H2NOC(O), or

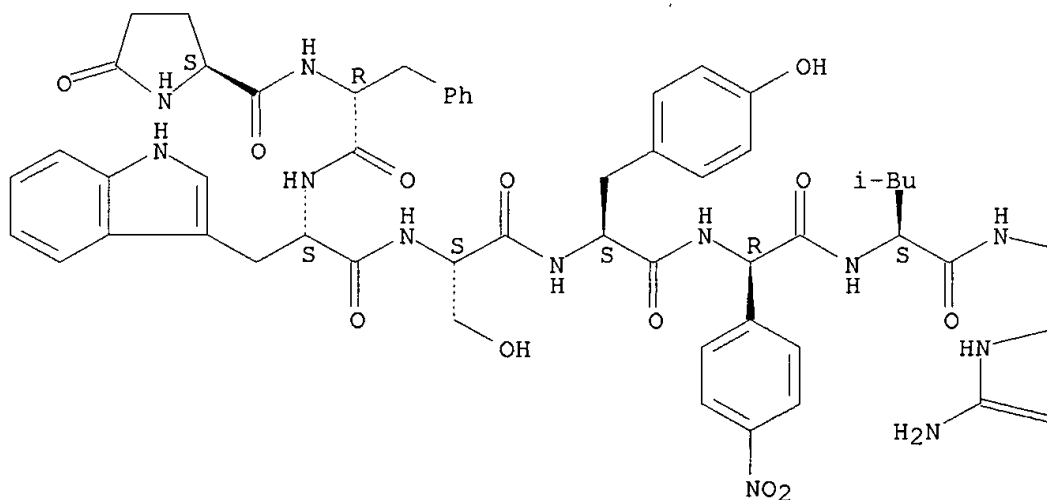


arylsulfonylcarbamoyl, etc.; G = NHCHRCHR1QC(O), NHCHRQ1CHRC(:Z); Z = O, S, H<sub>2</sub>; R = H, OH, C1-4 alkoxy, NH<sub>2</sub>, etc.; R1 = OH, (un)substituted NH<sub>2</sub>; Q = (un)substituted C3-7 alicyclic, benzene, or 5- to 7-membered heterocyclic ring; Q1 = CH(OH)CHR, CH<sub>2</sub>NH, P(O)(OH)CH<sub>2</sub>, CH(OH), etc.; B = null, NHCHRC(:Z); J = OH, NH<sub>2</sub>, (un)substituted C1-6 alkoxy or C1-6 alkylamino, etc.], are prepd. Thus, condensation of a hexanoic acid deriv. (II; R<sub>2</sub> = SiMe<sub>2</sub>CMe<sub>3</sub>, R<sub>3</sub> = OH, BOC = Me<sub>3</sub>CO<sub>2</sub>C) (prepn. given) with H-Leu-Phe-NH<sub>2</sub>.HCl.1/2H<sub>2</sub>O in the presence of 1-hydroxybenzotriazole.H<sub>2</sub>O, dimethyl-3-(3-dimethylaminopropyl)carbodiimide.HCl, and Et<sub>3</sub>N in DMF gave, after disilylation with Bu<sub>4</sub>NF in THF, II (R<sub>2</sub> = H, R<sub>3</sub> = Leu-Phe-NH<sub>2</sub>). The latter compd. inhibited synthetic and Escherichia coli-expressed HIV protease with IC<sub>50</sub> values of 2 and 0.6 nM, resp. Approx. 130 I were prepd.

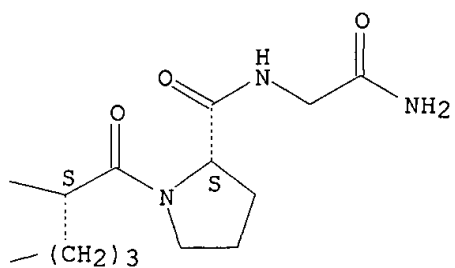
L4 ANSWER 100 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1990:172583 CAPLUS  
 DN 112:172583  
 TI Comparison of the hormonal and behavioral effect of LH-RH and its analogs  
 AU Makusheva, V. P.; Bakharev, V. D.; Nikolaev, S. V.; Lupanova, G. E.  
 CS Inst. Akush. Ginekol., Leningrad, USSR  
 SO Problemy Endokrinologii (1990), 36(1), 72-4  
 CODEN: PROEAS; ISSN: 0375-9660  
 DT Journal  
 LA Russian  
 IT **126609-80-1 126609-83-4**  
 RL: BIOL (Biological study)  
 (learning and ovulation and stress response to)  
 RN 126609-80-1 CAPLUS  
 CN Luteinizing hormone-releasing factor (swine), 2-D-phenylalanine-6-(4-nitro-D-phenylalanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

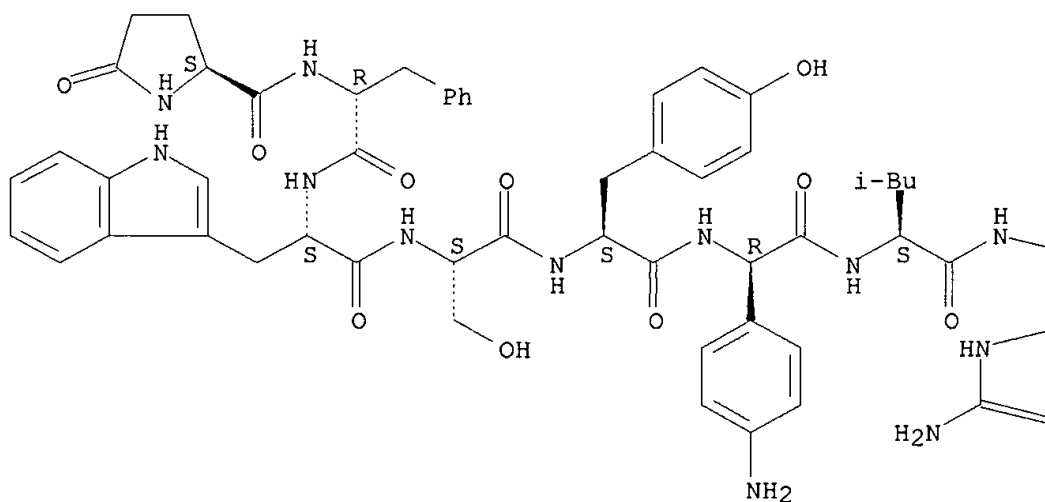


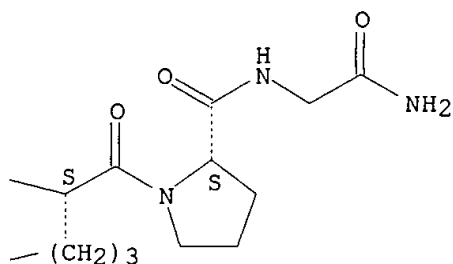
RN 126609-83-4 CAPLUS

CN Luteinizing hormone-releasing factor (swine), 2-D-phenylalanine-6-(4-amino-D-phenylalanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





=NH

AB LH-RH and 9 analogs were compared for their abilities to induce ovulation in immature and mature rats, for their effects on learning, and for their abilities to reduce the response to immobilization stress. Like LH-RH, the 3 analogs pGlu-His-Trp-Ser-Tyr-X-Leu-Arg-Pro-Gly-NH<sub>2</sub>, where X = D-Phe, D-Phe(NH<sub>2</sub>), and D-Phe(NO<sub>2</sub>), stimulated ovulation, accelerated learning, and attenuated responses to the stress. The 3 LH-RH analog antagonists which inhibited ovulation, pGlu-X-Trp-Ser-Tyr-D-Phe-Leu-Arg-Pro-Gly-NH<sub>2</sub>, where X = D-Phe, D-Phe(NO<sub>2</sub>), and D-Phe(NH<sub>2</sub>), had even greater effects than LH-RH and the agonist analogs. The analogs pGlu-His-Trp-OH, Ser-Tyr-D-Phe(NO<sub>2</sub>)-Leu-Arg-Pro-Gly-NH<sub>2</sub>, and pGlu-His-Trp-Ser-Tyr-Arg-Pro-Gly-NH<sub>2</sub> were essentially inactive.

L4 ANSWER 101 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1990:139785 CAPLUS

DN 112:139785

TI Synthesis and biological activities of new analogs of dermorphin substituted at position-2

AU Sivanandaiah, K. M.; Gurusiddappa, S.; Babu, V. V. Suresh

CS Cent. Coll., Bangalore Univ., Bangalore, 560 001, India

SO Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1989), 28B(4), 338-41

CODEN: IJSBDB; ISSN: 0376-4699

DT Journal

LA English

OS CASREACT 112:139785

IT **125943-14-8P**

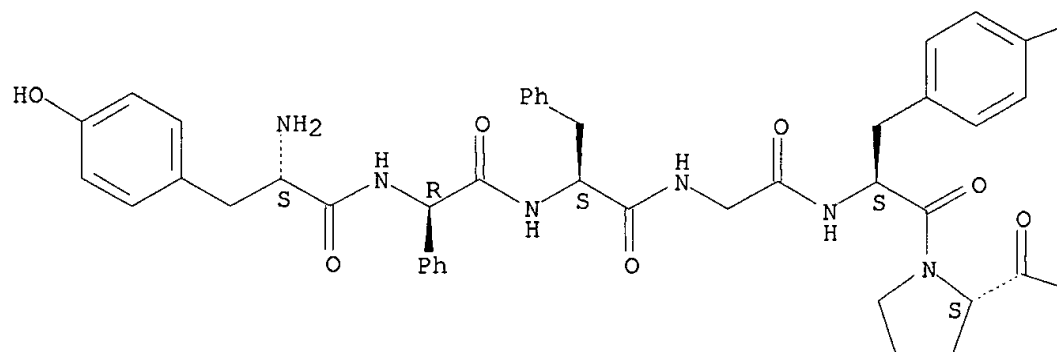
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and analgesic and antidiarrheal activities of)

RN 125943-14-8 CAPLUS

CN Dermorphin, 2-(D-2-phenylglycine)- (9CI) (CA INDEX NAME)

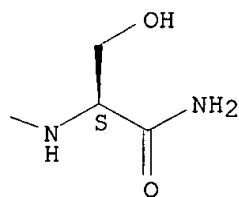
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

—OH

IT **125943-07-9P**

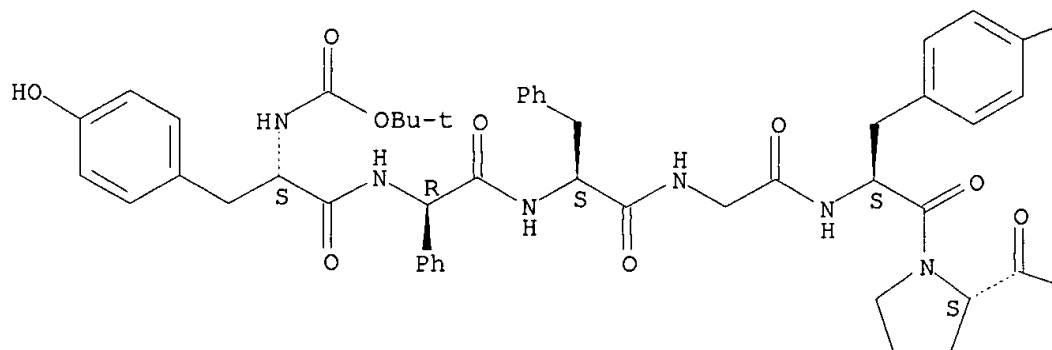
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and deblocking of, with formic acid)

RN 125943-07-9 CAPLUS

CN Dermorphin, N-[(1,1-dimethylethoxy)carbonyl]-2-(D-2-phenylglycine)- (9CI)  
(CA INDEX NAME)

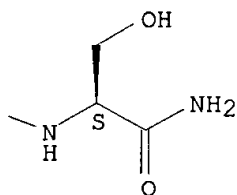
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

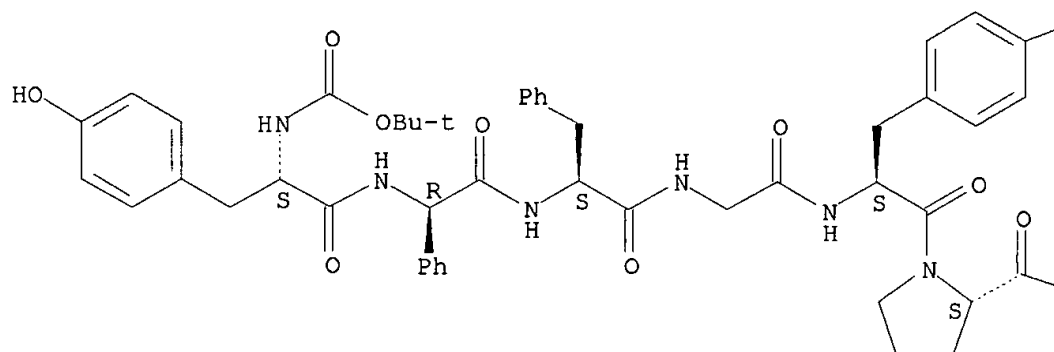
—OH



IT **125943-00-2DP**, ester with Merrifield resin  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and resin cleavage-amidation of, with ammonia)  
 RN 125943-00-2 CAPLUS  
 CN Dermorphin, N-[(1,1-dimethylethoxy)carbonyl]-2-(D-2-phenylglycine)-7-L-serine- (9CI) (CA INDEX NAME)

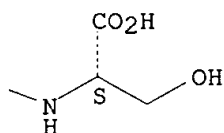
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

—OH



AB Seven analogs of demorphin with different D-amino acids at position 2 have been obtained by the solid-phase method using mainly 9-fluorenylmethoxycarbonyl amino acid active esters in the presence of 1-hydroxybenzotriazole, the solid support being the Merrifield resin. Their pharmacol. effects have been studied in vitro by the guinea pig ileum (GPI) assay and in vivo by the hot plate method. The antidiarrheal properties of these peptides have also studied in mice (in vivo). [D-Nva2]- and [D-Eth2]-dermorphin (Nva = norvaline; Eth = ethionine) approach morphine in the GPI assay and hot plate test resp. Though, in general, replacement of D-Ala2 by other D-amino acids leads to lower GPI and analgesic activities, there is an enhancement of antidiarrheal potency in the case of four analogs, the most active one being [D-Phe2]-dermorphin, which is 2.7 times more potent than morphine.

L4 ANSWER 102 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1990:119450 CAPLUS

DN 112:119450

TI Preparation of neurotensin fragment analogs as central nervous system agents and pharmaceutical compositions containing them

IN Tsuchiya, Yutaka; Sasaki, Atsushi; Yoshino, Hiroshi; Karibe, Norio; Sugimoto, Hachiro; Kubota, Atsuhiko; Kosasa, Michiko; Araki, Shin; Ikeda, Masuhiro; et al.

PA Eisai Co., Ltd., Japan

SO Eur. Pat. Appl., 55 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 333071   | A2   | 19890920 | EP 1989-104302  | 19890310 |
|    | EP 333071   | A3   | 19900926 |                 |          |
|    | R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE |      |          |                 |          |
|    | FI 8900918  | A    | 19890912 | JP 1988-57985   | 19880311 |
|    |   |      |          | FI 1989-918     | 19890227 |
|    |   |      |          | JP 1988-57985   | 19880311 |
|    | AU 8931083  | A1   | 19890914 | AU 1989-31083   | 19890307 |
|    |   |      |          | JP 1988-57985   | 19880311 |
|    | JP 01316399                                       | A2   | 19891221 | JP 1989-55941   | 19890308 |
|    |   |      |          | JP 1988-57985   | 19880311 |
|    | NO 8901006  | A    | 19890912 | NO 1989-1006    | 19890309 |
|    |   |      |          | JP 1988-57985   | 19880311 |
|    | DK 8901169  | A    | 19890912 | DK 1989-1169    | 19890310 |
|    |   |      |          | JP 1988-57985   | 19880311 |
|    | HU 49370  | A2   | 19890928 | HU 1989-1180    | 19890310 |
|    | HU 199879   | B    | 19900328 |                 |          |
|    |   |      |          | JP 1988-57985   | 19880311 |

IT 125600-89-7P

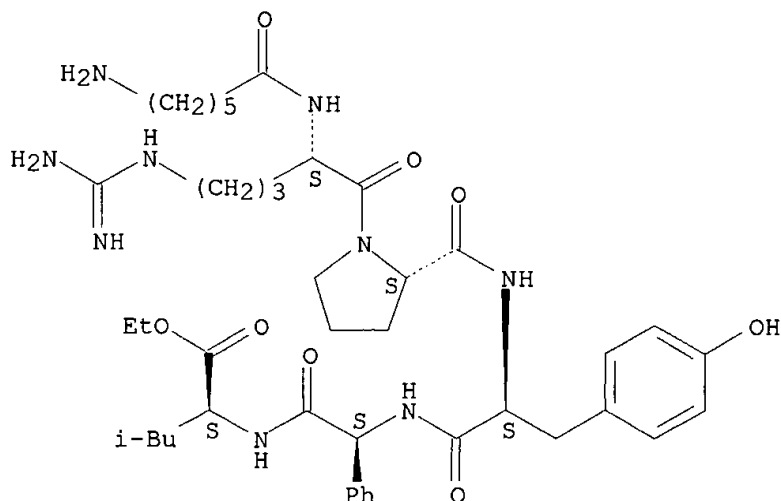
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. of, as central nervous system agent)

RN 125600-89-7 CAPLUS

CN L-Leucine, N-[N-[N-[1-[N2-(6-amino-1-oxohexyl)-L-arginyl]-L-prolyl]-L-tyrosyl]-L-2-phenylglycyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB A-B-C-D-E-F-R1; [A = amino acid residue, guanidinoalkylcarbonyl, piperidinyllalkylcarbonyl, aminoalkylcarbonyl; B, E, F = amino acid

residue, residue of an alkyl deriv. of amino acid; C = L-Pro or deriv.; D = L-amino acid residue; R1 = (substituted) amino] useful as central nervous system agents (antipsychotics, analgesics) were prepd. H-Gb-Arg-Pro-Trp-Pgl-Leu-OEt (II; Gb = residue of .omega.-guanidinobutanoic acid, Pgl = phenylglycine residue) was prepd. in many steps by the soln. method starting from BOC-Pgl-OH and H-Leu-OEt.HCl. II at 0.2 mg/kg s.c. showed 20.6% antagonism of methamphetamine in mice.

L4 ANSWER 103 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1990:118534 CAPLUS

DN 112:118534

TI Preparation of 1-sulfo-2-oxoazetidines as antibacterial agents

IN Ochiai, Michihiko; Kishimoto, Shoji; Matsuo, Taisuke

PA Takeda Chemical Industries, Ltd., Japan

SO U.S., 252 pp. Cont.-in-part of U.S. Ser. No. 326,938.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 6

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|-------------|------|----------|-----------------|----------|
| PI | US 4782147  | A    | 19881101 | US 1983-499802  | 19830531 |
|    |             |      |          | WO 1980-JP297   | 19801205 |
|    |             |      |          | WO 1981-JP103   | 19810430 |
|    |             |      |          | WO 1981-JP183   | 19810821 |
|    |             |      |          | WO 1981-JP252   | 19810924 |
|    |             |      |          | US 1981-326938  | 19811203 |
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|    | WO 8201873  | A1   | 19820610 | WO 1980-JP297   | 19801205 |
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|    | WO 8203859  | A1   | 19821111 | WO 1981-JP103   | 19810430 |
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|    | WO 8300689  | A1   | 19830303 | WO 1981-JP183   | 19810821 |
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|    | WO 8301063  | A1   | 19830331 | WO 1981-JP252   | 19810924 |
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|    | US 4822788  | A    | 19890418 | US 1981-326938  | 19811203 |
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|    |             |      |          | WO 1981-JP103   | 19810430 |
|    |             |      |          | WO 1981-JP183   | 19810821 |
|    |             |      |          | WO 1981-JP252   | 19810924 |
|    | JP 58210061 | A2   | 19831207 | JP 1982-93463   | 19820531 |
|    | JP 0406865  | B4   | 19921026 |                 |          |
|    | US 4572801  | A    | 19860225 | US 1983-499801  | 19830531 |
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|    |             |      |          | WO 1981-WO252   | 19810924 |
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|    |             |      |          | JP 1982-93463   | 19820531 |
|    |             |      |          | US 1982-405592  | 19820805 |
|    | GB 2156350  | A1   | 19851009 | GB 1985-9070    | 19850409 |
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|    |             |      |          | JP 1982-73728   | 19820430 |
|    |             |      |          | JP 1982-93463   | 19820531 |
|    |             |      |          | GB 1983-10520   | 19830419 |
|    | NO 8700981  | A    | 19831031 | NO 1987-981     | 19870310 |



FI 8801563 A 19880405

JP 1982-73728 19820430  
 JP 1982-93463 19820531  
 NO 1983-1514 19830429  
 FI 1988-1563 19880405  
 JP 1982-73728 19820430  
 JP 1982-93463 19820531  
 FI 1983-1457 19830428

PATENT FAMILY INFORMATION:

FAN 1982:562692

|    | PATENT NO.                        | KIND | DATE     | APPLICATION NO. | DATE     |
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| PI | WO 8201551<br>W: MC               | A1   | 19820513 | WO 1980-JP255   | 19801023 |
|    | EP 50965<br>R: CH, DE, FR, GB, IT | A1   | 19820505 | EP 1981-304996  | 19811023 |
|    | JP 57098258                       | A2   | 19820618 | WO 1980-JP255   | 19801023 |
|    | JP 04024326                       | B4   | 19920424 | WO 1980-JP295   | 19801204 |
|    |                                   |      |          | JP 1981-170634  | 19811023 |
|    | US 4725591                        | A    | 19880216 | WO 1980-JP255   | 19801023 |
|    |                                   |      |          | US 1984-576776  | 19840203 |
|    |                                   |      |          | WO 1980-JP255   | 19801023 |
|    |                                   |      |          | WO 1980-JP295   | 19801204 |
|    |                                   |      |          | US 1981-314512  | 19811023 |

FAN 1982:562701

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| PI | WO 8201820<br>W: MC               | A1   | 19820610 | WO 1980-JP295   | 19801204 |
|    | EP 50965<br>R: CH, DE, FR, GB, IT | A1   | 19820505 | EP 1981-304996  | 19811023 |
|    | CA 1338539                        | A1   | 19960820 | WO 1980-JP255   | 19801023 |
|    |                                   |      |          | WO 1980-JP295   | 19801204 |
|    |                                   |      |          | CA 1981-391401  | 19811203 |
|    |                                   |      |          | WO 1980-JP295   | 19801204 |
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|    |                                   |      |          | WO 1981-JP103   | 19810430 |
|    |                                   |      |          | WO 1981-JP183   | 19810821 |
|    |                                   |      |          | WO 1981-JP252   | 19810924 |
|    |                                   |      |          | EP 1981-304996  | 19811023 |
|    |                                   |      |          | JP 1981-170634  | 19811023 |
|    | US 4725591                        | A    | 19880216 | US 1984-576776  | 19840203 |
|    |                                   |      |          | WO 1980-JP255   | 19801023 |
|    |                                   |      |          | WO 1980-JP295   | 19801204 |
|    |                                   |      |          | US 1981-314512  | 19811023 |

FAN 1982:598037

|    | PATENT NO.          | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---------------------|------|----------|-----------------|----------|
| PI | WO 8201873<br>W: MC | A1   | 19820610 | WO 1980-JP297   | 19801205 |
|    | IL 64315            | A1   | 19880429 | IL 1981-64315   | 19811119 |
|    |                     |      |          | WO 1980-JP297   | 19801205 |
|    |                     |      |          | WO 1981-JP103   | 19810430 |
|    |                     |      |          | WO 1981-JP183   | 19810821 |
|    |                     |      |          | WO 1981-JP252   | 19810924 |
|    | AU 8177829          | A1   | 19820610 | AU 1981-77829   | 19811125 |
|    | AU 557689           | B2   | 19870108 |                 |          |

|             |    |          |                 |          |
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|             |    |          | WO 1980-JP297   | 19801205 |
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|             |    |          | WO 1981-JP183   | 19810821 |
|             |    |          | WO 1981-JP252   | 19810924 |
| HU 31125    | O  | 19840428 | HU 1981-3577    | 19811126 |
| HU 194870   | B  | 19880328 |                 |          |
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| CS 253565   | B2 | 19871112 | CS 1981-8834    | 19811130 |
|             |    |          | WO 1980-JP297   | 19801205 |
| DK 8105344  | A  | 19820606 | DK 1981-5344    | 19811202 |
|             |    |          | WO 1980-JP297   | 19801205 |
|             |    |          | WO 1981-JP103   | 19810430 |
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| FI 81085    | B  | 19900531 |                 |          |
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|             |    |          | WO 1980-JP297   | 19801205 |
|             |    |          | WO 1981-JP103   | 19810430 |
|             |    |          | WO 1981-JP183   | 19810821 |
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| NO 160577   | B  | 19890123 |                 |          |
| NO 160577   | C  | 19890503 |                 |          |
|             |    |          | WO 1980-JP297   | 19801205 |
|             |    |          | WO 1981-JP103   | 19810430 |
|             |    |          | WO 1981-JP183   | 19810821 |
|             |    |          | WO 1981-JP252   | 19810924 |
| SU 1396962  | A3 | 19880515 | SU 1981-3364401 | 19811202 |
|             |    |          | WO 1980-JP297   | 19801205 |
| JP 01003189 | B4 | 19890119 | JP 1981-194311  | 19811202 |
|             |    |          | WO 1980-JP297   | 19801205 |
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|             |    |          | WO 1981-JP183   | 19810821 |
|             |    |          | WO 1981-JP252   | 19810924 |
| BR 8107866  | A  | 19820908 | BR 1981-7866    | 19811203 |
|             |    |          | WO 1980-JP297   | 19801205 |
| US 4550105  | A  | 19851029 | US 1981-326937  | 19811203 |
|             |    |          | WO 1980-JP297   | 19801205 |
|             |    |          | WO 1981-JP103   | 19810430 |
|             |    |          | WO 1981-JP183   | 19810821 |
|             |    |          | WO 1981-JP252   | 19810924 |
| US 4822788  | A  | 19890418 | US 1981-326938  | 19811203 |
|             |    |          | WO 1980-JP297   | 19801205 |
|             |    |          | WO 1981-JP103   | 19810430 |
|             |    |          | WO 1981-JP183   | 19810821 |
|             |    |          | WO 1981-JP252   | 19810924 |
| CA 1338539  | A1 | 19960820 | CA 1981-391401  | 19811203 |
|             |    |          | WO 1980-JP295   | 19801204 |
|             |    |          | WO 1980-JP297   | 19801205 |
|             |    |          | WO 1981-JP103   | 19810430 |
|             |    |          | WO 1981-JP183   | 19810821 |
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|             |    |          | EP 1981-304996  | 19811023 |

|            |    |          |                                       |          |
|------------|----|----------|---------------------------------------|----------|
| BE 891366  | A1 | 19820604 | JP 1981-170634                        | 19811023 |
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|            |    |          | WO 1980-JP297                         | 19801205 |
|            |    |          | WO 1981-JP103                         | 19810430 |
|            |    |          | WO 1981-JP183                         | 19810821 |
|            |    |          | WO 1981-JP252                         | 19810924 |
|            |    |          | SE 1981-7274                          | 19811204 |
| SE 8107274 | A  | 19820606 |                                       |          |
| SE 457256  | B  | 19881212 |                                       |          |
| SE 457256  | C  | 19890413 |                                       |          |
|            |    |          | WO 1980-JP297                         | 19801205 |
|            |    |          | WO 1981-JP103                         | 19810430 |
|            |    |          | WO 1981-JP183                         | 19810821 |
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| FR 2495613 | A1 | 19820611 | FR 1981-22775                         | 19811204 |
| FR 2495613 | B1 | 19850809 |                                       |          |
|            |    |          | WO 1980-JP297                         | 19801205 |
|            |    |          | WO 1981-JP103                         | 19810430 |
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| EP 53816   | A1 | 19820616 | EP 1981-110155                        | 19811204 |
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|            |    |          | WO 1980-JP297                         | 19801205 |
|            |    |          | WO 1981-JP103                         | 19810430 |
|            |    |          | WO 1981-JP183                         | 19810821 |
|            |    |          | WO 1981-JP252                         | 19810924 |
| NL 8105470 | A  | 19820701 | NL 1981-5470                          | 19811204 |
|            |    |          | WO 1980-JP297                         | 19801205 |
|            |    |          | WO 1981-JP103                         | 19810430 |
|            |    |          | WO 1981-JP183                         | 19810821 |
|            |    |          | WO 1981-JP252                         | 19810924 |
| GB 2091724 | A  | 19820804 | GB 1981-36619                         | 19811204 |
| GB 2091724 | B2 | 19850731 |                                       |          |
|            |    |          | WO 1980-JP297                         | 19801205 |
|            |    |          | WO 1981-JP103                         | 19810430 |
|            |    |          | WO 1981-JP183                         | 19810821 |
|            |    |          | WO 1981-JP252                         | 19810924 |
| DE 3148021 | A1 | 19821021 | DE 1981-3148021                       | 19811204 |
|            |    |          | WO 1980-JP297                         | 19801205 |
|            |    |          | WO 1981-JP103                         | 19810430 |
|            |    |          | WO 1981-JP183                         | 19810821 |
|            |    |          | WO 1981-JP252                         | 19810924 |
| ZA 8108444 | A  | 19821027 | ZA 1981-8444                          | 19811204 |
| ES 507715  | A1 | 19830201 | WO 1980-JP297                         | 19801205 |
|            |    |          | ES 1981-507715                        | 19811204 |
|            |    |          | WO 1980-JP297                         | 19801205 |
| AT 8105208 | A  | 19850215 | AT 1981-5208                          | 19811204 |
| AT 378768  | B  | 19850925 |                                       |          |
|            |    |          | WO 1980-JP297                         | 19801205 |
|            |    |          | WO 1981-JP103                         | 19810430 |
|            |    |          | WO 1981-JP183                         | 19810821 |
|            |    |          | WO 1981-JP252                         | 19810924 |
| CH 657610  | A  | 19860915 | CH 1981-7787                          | 19811204 |
|            |    |          | WO 1980-JP297                         | 19801205 |
|            |    |          | WO 1981-JP103                         | 19810430 |
|            |    |          | WO 1981-JP183                         | 19810821 |
|            |    |          | WO 1981-JP252                         | 19810924 |

|            |    |          |                 |          |
|------------|----|----------|-----------------|----------|
| AT 33981   | E  | 19880515 | AT 1981-110155  | 19811204 |
|            |    |          | WO 1980-JP297   | 19801205 |
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|            |    |          | WO 1981-JP252   | 19810924 |
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| WO 8202043 | A1 | 19820624 | WO 1981-JP369   | 19811205 |
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|            |    |          | WO 1980-JP297   | 19801205 |
|            |    |          | WO 1981-JP103   | 19810430 |
|            |    |          | WO 1981-JP183   | 19810821 |
|            |    |          | WO 1981-JP252   | 19810924 |
| US 4675397 | A  | 19870623 | US 1982-405592  | 19820805 |
|            |    |          | WO 1980-JP297   | 19801205 |
|            |    |          | WO 1981-JP103   | 19810430 |
|            |    |          | WO 1981-JP183   | 19810821 |
|            |    |          | WO 1981-JP252   | 19810924 |
|            |    |          | US 1981-326938  | 19811203 |
|            |    |          | JP 1982-73728   | 19820430 |
| ES 516254  | A1 | 19831016 | ES 1982-516254  | 19821006 |
|            |    |          | WO 1980-JP297   | 19801205 |
|            |    |          | WO 1981-JP103   | 19810430 |
|            |    |          | WO 1981-JP183   | 19810821 |
|            |    |          | WO 1981-JP252   | 19810924 |
| CS 253572  | B2 | 19871112 | CS 1982-7585    | 19821025 |
|            |    |          | WO 1980-JP297   | 19801205 |
|            |    |          | CS 1981-8834    | 19811130 |
| SU 1484294 | A3 | 19890530 | SU 1983-3556253 | 19830215 |
|            |    |          | WO 1980-JP297   | 19801205 |
| US 4782147 | A  | 19881101 | US 1983-499802  | 19830531 |
|            |    |          | WO 1980-JP297   | 19801205 |
|            |    |          | WO 1981-JP103   | 19810430 |
|            |    |          | WO 1981-JP183   | 19810821 |
|            |    |          | WO 1981-JP252   | 19810924 |
|            |    |          | US 1981-326938  | 19811203 |
| AT 8401647 | A  | 19860515 | JP 1982-93463   | 19820531 |
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| US 4665067 | A  | 19870512 | US 1985-741741  | 19850605 |
|            |    |          | WO 1980-JP297   | 19801205 |
|            |    |          | WO 1981-JP103   | 19810430 |
|            |    |          | WO 1981-JP183   | 19810821 |
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|            |    |          | US 1981-326938  | 19811203 |
| US 4673739 | A  | 19870616 | US 1985-778219  | 19850918 |
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|     |   |      |          |                 |          |
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|     |   |      |          | US 1982-405592  | 19820805 |
|     |   |      |          | US 1983-499801  | 19830531 |
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| PI  | EP 53816                                  | A1   | 19820616 | EP 1981-110155  | 19811204 |
|     | EP 53816                                  | B1   | 19880504 |                 |          |
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|     |   |      |          | WO 1980-JP297   | 19801205 |
|     |   |      |          | WO 1981-JP103   | 19810430 |
|     |   |      |          | WO 1981-JP183   | 19810821 |
|     |   |      |          | WO 1981-JP252   | 19810924 |
|     | WO 8201873                                | A1   | 19820610 | WO 1980-JP297   | 19801205 |
|     | W: MC                                     |      |          |                 |          |
|     | WO 8203859                                | A1   | 19821111 | WO 1981-JP103   | 19810430 |
|     | W: MC                                     |      |          |                 |          |
|     | WO 8300689                                | A1   | 19830303 | WO 1981-JP183   | 19810821 |
|     | W: MC                                     |      |          |                 |          |
|     | WO 8301063                                | A1   | 19830331 | WO 1981-JP252   | 19810924 |
|     | W: MC                                     |      |          |                 |          |
|     | AT 33981                                  | E    | 19880515 | AT 1981-110155  | 19811204 |
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|     |   |      |          | WO 1981-JP103   | 19810430 |
|     |   |      |          | WO 1981-JP183   | 19810821 |
|     |   |      |          | WO 1981-JP252   | 19810924 |
|     |   |      |          | EP 1981-110155  | 19811204 |
| FAN | 1984:209515                               |      |          |                 |          |
|     | PATENT NO.                                | KIND | DATE     | APPLICATION NO. | DATE     |
| PI  | EP 93376                                  | A2   | 19831109 | EP 1983-104061  | 19830426 |
|     | EP 93376                                  | A3   | 19861015 |                 |          |
|     | EP 93376                                  | B1   | 19900321 |                 |          |
|     | EP 93376                                  | B2   | 19990407 |                 |          |
|     | R: AT, BE, CH, DE, FR, IT, LI, LU, NL, SE |      |          |                 |          |
|     |   |      |          | JP 1982-73728   | 19820430 |
|     |   |      |          | JP 1982-93463   | 19820531 |
|     | JP 58189176                               | A2   | 19831104 | JP 1982-73728   | 19820430 |
|     | JP 63034155                               | B4   | 19880708 |                 |          |
|     | JP 58210061                               | A2   | 19831207 | JP 1982-93463   | 19820531 |
|     | JP 04066865                               | B4   | 19921026 |                 |          |
|     | AU 8313445                                | A1   | 19831103 | AU 1983-13445   | 19830412 |
|     | AU 564150                                 | B2   | 19870806 |                 |          |
|     |   |      |          | JP 1982-73728   | 19820430 |
|     |   |      |          | JP 1982-93463   | 19820531 |
|     | ZA 8302742                                | A    | 19831228 | ZA 1983-2742    | 19830419 |
|     |   |      |          | JP 1982-73728   | 19820430 |
|     | GB 2124207                                | A1   | 19840215 | GB 1983-10520   | 19830419 |
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|     | AT 51223                                  | E    | 19900415 | AT 1983-104061  | 19830426 |
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|     |   |      |          | EP 1983-104061  | 19830426 |
|     | DK 8301889                                | A    | 19831031 | DK 1983-1889    | 19830428 |
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|             |    |          |                 |          |
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| US 4572801  | A  | 19860225 | US 1983-499801  | 19830531 |
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|             |    |          | GB 1983-10520   | 19830419 |
| ES 543809   | A1 | 19860901 | ES 1985-543809  | 19850601 |
|             |    |          | JP 1982-73728   | 19820430 |
|             |    |          | JP 1982-93463   | 19820531 |
| SU 1380612  | A3 | 19880307 | SU 1985-3909204 | 19850620 |
|             |    |          | JP 1982-73728   | 19820430 |
| ES 551942   | A1 | 19871016 | ES 1986-551942  | 19860213 |
|             |    |          | JP 1982-73728   | 19820430 |
|             |    |          | JP 1982-93463   | 19820531 |
| JP 62215586 | A2 | 19870922 | JP 1987-28496   | 19870210 |
| JP 03021542 | B4 | 19910322 |                 |          |

|            |   |          |               |          |
|------------|---|----------|---------------|----------|
| NO 8700981 | A | 19831031 | JP 1982-73728 | 19820430 |
|            |   |          | NO 1987-981   | 19870310 |
|            |   |          | JP 1982-73728 | 19820430 |
|            |   |          | JP 1982-93463 | 19820531 |
| FI 8801563 | A | 19880405 | NO 1983-1514  | 19830429 |
|            |   |          | FI 1988-1563  | 19880405 |
|            |   |          | JP 1982-73728 | 19820430 |
|            |   |          | JP 1982-93463 | 19820531 |
|            |   |          | FI 1983-1457  | 19830428 |

OS MARPAT 112:118534

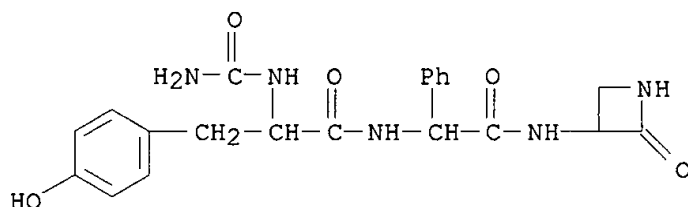
IT **122666-89-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

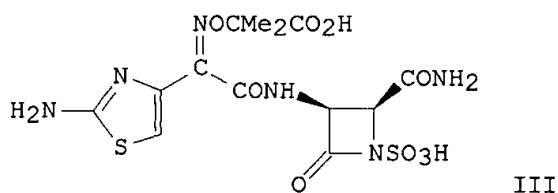
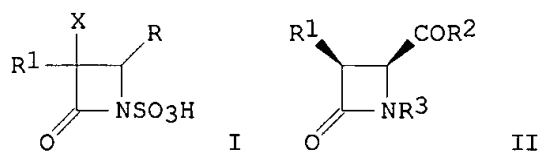
(prepn. and reaction of, in prepn. of antibacterial agents)

RN 122666-89-1 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-D-tyrosyl-N-(2-oxo-3-azetidiny)-D-2-phenyl-(9CI) (CA INDEX NAME)



GI



AB The title compds. [I; R = H, N3, halo, NH2, acylamino, OR5, SOnR5, P(O)(OR5)2, SSR5, C-attached org. residue; R1 = (protected) NH2, acylamino; R5 = org. residue; X = H, MeO; n = 0-2] and their salts were prepd. 2-Oxoazetidine II [R1 = PhCH2O2CNH, R2 = OMe, R3 = 2,4-(MeO)2C6H3CH2] (prepn. from corresponding 3-amino deriv. given) was stirred 3 h at 90-95.degree. with K2S2O8 in aq. MeCN contg. K2HPO4 to give II (R1 and R2 as above, R3 = H) which was stirred 19 h in THF contg. aq. NH3 to give II (R1 as above, R2 = NH2, R3 = H). The latter was hydrogenolyzed over Pd/C and the product stirred with 4-O2NC6H4CH2O2CCMe2ON:CQCOC1 [Q = 2-(2-chloroacetamido)-4-thiazolyl] (prepn.

given) to give II (R1 = 4-O2NC6H4CH2O2CCMe2ON:CQCONH, R2 = NH2, R3 = H) which was treated overnight at 4.degree. with SO3.DMF in DMF to give, after ion-exchange chromatog., II (R1, R2 unchanged, R3 = SO3Na). Deprotection of the latter in 2 steps gave title compd. III, which had min. inhibitory concn. of 1.56 and 0.39 .mu.g/mL against *Enterobacter cloacae* IFO 129537 and *Klebsiella pneumoniae* TN 1711, resp.

L4 ANSWER 104 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1989:601478 CAPLUS

DN 111:201478

TI Improved delivery through biological membranes. XLI. Brain-enhanced delivery of chlorambucil

AU Bodor, Nicholas; Venkatraghavan, Vasudevan; Winwood, David; Estes, Kerry; Brewster, Marcus E.

CS Pharmatec. Inc., Alachua, FL, 32615, USA

SO International Journal of Pharmaceutics (1989), 53(3), 195-208

CODEN: IJPHDE; ISSN: 0378-5173

DT Journal

LA English

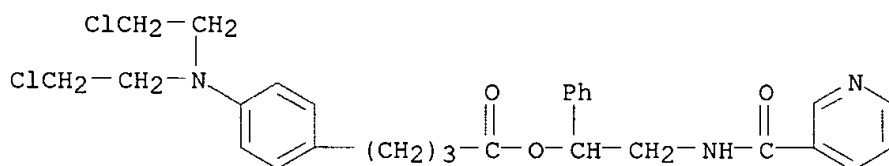
IT **123630-97-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and quaternization of, with Me sulfate)

RN 123630-97-7 CAPLUS

CN Benzenebutanoic acid, 4-[bis(2-chloroethyl)amino]-, 1-phenyl-2-[(3-pyridinylcarbonyl)amino]ethyl ester (9CI) (CA INDEX NAME)



IT **123630-90-0P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and redn. of, in brain-enhanced delivery of chlorambucil)

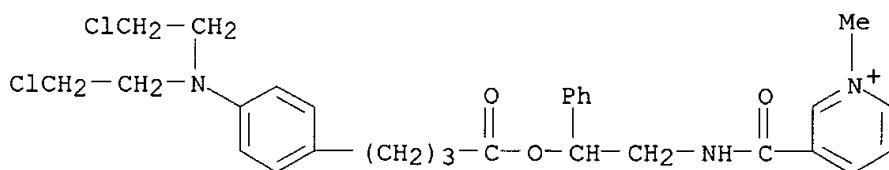
RN 123630-90-0 CAPLUS

CN Pyridinium, 3-[[[2-[4-[4-[bis(2-chloroethyl)amino]phenyl]-1-oxobutoxy]-2-phenylethyl]amino]carbonyl]-1-methyl-, methyl sulfate (9CI) (CA INDEX NAME)

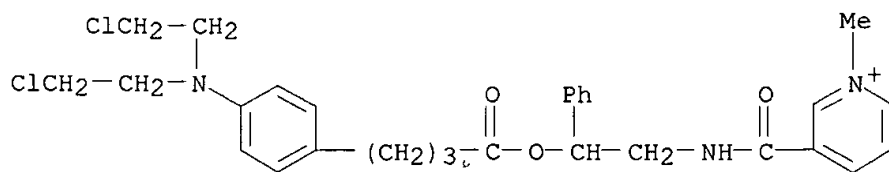
CM 1

CRN 123630-89-7

CMF C29 H34 Cl2 N3 O3







CM 2

CRN 21228-90-0

CMF C H3 O4 S

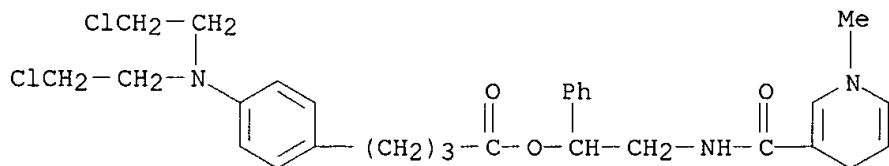
Me-O-SO<sub>3</sub><sup>-</sup>

IT 123630-82-0P

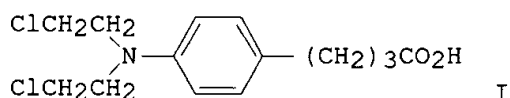
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, as brain-enhanced delivery system for chlorambucil)

RN 123630-82-0 CAPLUS

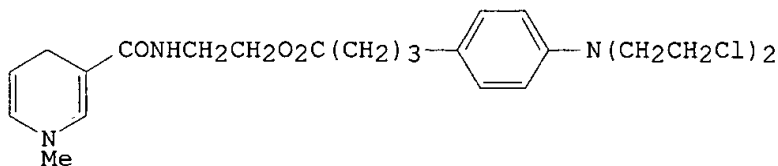
CN Benzenebutanoic acid, 4-[bis(2-chloroethyl)amino]-, 2-[[[(1,4-dihydro-1-methyl-3-pyridinyl)carbonyl]amino]-1-phenylethyl ester (9CI) (CA INDEX NAME)



GI



I



II

AB Brain-enhanced delivery of chlorambucil (I) was achieved using a dihydropyridine pyridinium salt chem. delivery system (CDS). Application of the CDS approach to the carboxylic acid-contg. anticancer agent required the development of novel, alc. redox carriers. Several N'-(.omega.-hydroxyalkyl), -(.omega.-hydroxycycloalkyl) and -(.omega.-hydroxy-branched alkyl)nicotinamide derivs. were therefore

synthesized. After in vitro characterization of the dihydropyridine delivery forms of I, these compds. were tested in vivo in the rat. The CDS deriv. in which an Et group sepd. the 1-methyl-1,4-dihydronicotinamide and I fragments generated sustained levels of I in the brains of test animals after i.v. administration ( $t_{1/2}$  in brain = 2.4 days), while blood levels rapidly fell ( $t_{1/2}$  = 2 h) producing a favorable brain/blood ratio. This compd. (II) was well tolerated at doses of 60 mg/kg, while equimolar I (39 mg/kg) caused >80% mortality in test animals within 2 h. Subsequently, a cyclohexyl-contg. CDS deriv. was tested. This sterically more hindered system produced a lower level of I in the periphery but also reduced central nervous system concn. of the drug.

L4 ANSWER 105 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1989:553339 CAPLUS

DN 111:153339

TI Preparation of esterified N-(dibenzocycloheptenyldieneethyl)ephedrine derivatives with prolonged antiulcer activity

IN Butelman, Federico

PA Etablissement Texcontor, Liechtenstein

SO Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 313885   | A1   | 19890503 | EP 1988-116449  | 19881005 |
|    | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                 |          |
|    | US 4935444  | A    | 19900619 | IT 1987-22407   | 19871023 |
|    |   |      |          | US 1988-254220  | 19881006 |
|    |   |      |          | IT 1987-22407   | 19871023 |
|    | JP 01135748   | A2   | 19890529 | JP 1988-264240  | 19881021 |
|    |   |      |          | IT 1987-22407   | 19871023 |
|    | US 4990522  | A    | 19910205 | US 1990-487277  | 19900302 |
|    |   |      |          | IT 1987-22407   | 19871023 |
|    |   |      |          | US 1988-254220  | 19881006 |

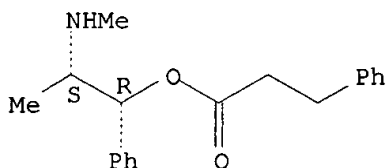
IT **122881-51-0P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and N-alkylation of, with (haloethylidene)dibenzocycloheptene)

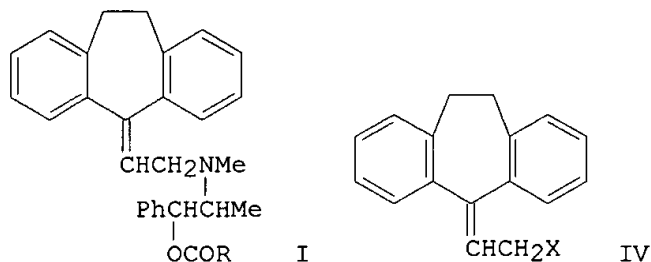
RN 122881-51-0 CAPLUS

CN Benzenepropanoic acid, 2-(methylamino)-1-phenylpropyl ester, [R-(R\*,S\*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB Title compds. [I; R = C<sub>9</sub>H<sub>19</sub>, C<sub>15</sub>H<sub>31</sub>, CH(NH<sub>2</sub>)(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H, (CH<sub>2</sub>)<sub>2</sub>Ph, CMe<sub>3</sub>, p-HOC<sub>6</sub>H<sub>4</sub>, 2-thienyl, 3-pyridyl, 1-amino-2-(5-imidazolyl)ethyl, pamoic acid residue] are prepd. by esterification of ephedrine (II) with RCOCl to give PhCH(O<sub>2</sub>CR)CHMeNHMe (III), followed by N-alkylation with a (haloethylidene)dibenzocycloheptene IV (X = halo). II was esterified by decanoyl chloride (prepd. from the acid) to give 65% III [R = Me(CH<sub>2</sub>)<sub>8</sub>], which was refluxed in MeCN with IV (X = halo, not specified) to give 54% I [R = MeC(CH<sub>2</sub>)<sub>2</sub>]. The latter inhibited stress-induced ulcers in rats with ED<sub>50</sub> of 0.4 and 2.1 mg/kg orally, administered 6 and 36 h prior to commencement of the stress, resp.

L4 ANSWER 106 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1989:115313 CAPLUS

DN 110:115313

TI Peptides related to leucine-/methionine-enkephalinamides: synthesis and biological activities

AU Sivanandaiah, K. M.; Gurusiddappa, S.; Suresh Babu, V. V.

CS Cent. Coll., Bangalore Univ., Bangalore, 560 001, India

SO Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1988), 27B(7), 645-8  
CODEN: IJSBDB; ISSN: 0376-4699

DT Journal

LA English.

OS CASREACT 110:115313

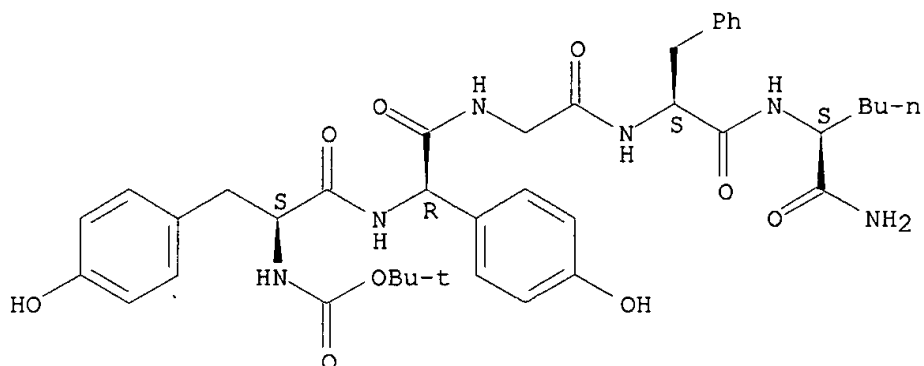
IT **119221-28-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and deblocking of, with formic acid and anisole)

RN 119221-28-2 CAPLUS

CN L-Norleucinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-tyrosyl-D-2-(4-hydroxyphenyl)glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



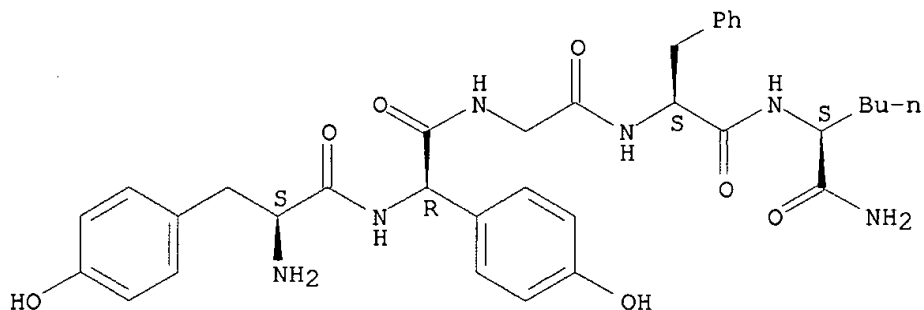
IT 119221-23-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and morphine-like, analgesic, and antidiarrheal activities of)

RN 119221-23-7 CAPLUS

CN L-Norleucinamide, L-tyrosyl-D-2-(4-hydroxyphenyl)glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



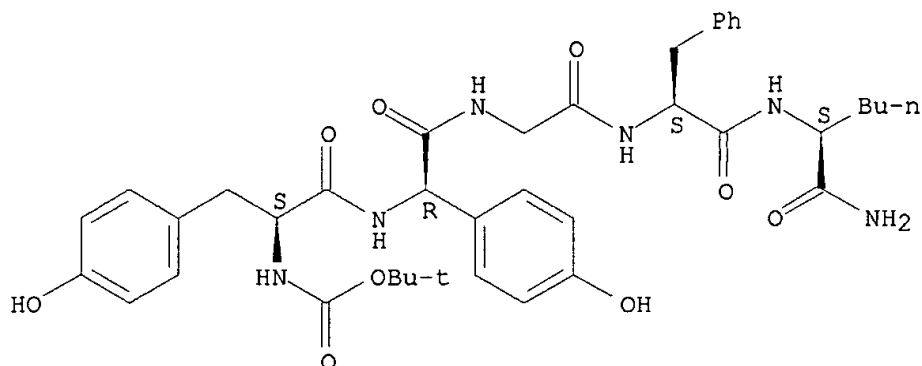
IT 119221-28-2DP, resin-bound

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and resin cleavage and side chain deblocking of, with ammonia)

RN 119221-28-2 CAPLUS

CN L-Norleucinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-tyrosyl-D-2-(4-hydroxyphenyl)glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Six analogs of leucine- and methionine-enkephalinamides have been synthesized by substitution of D-amino acids at position 2 and Nle or Eth (Eth = ethionine) at position 5 by solid phase techniques employing the base labile 9-fluorenylmethoxycarbonyl group for N.alpha. protection. One of the analogs, H-Tyr-D-Nva-Gly-Phe-Eth-NH<sub>2</sub>, is 21.6 times more potent than morphine in the guinea pig ileum assay.

L4 ANSWER 107 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1989:58089 CAPLUS

DN 110:58089

TI Potent angiotensin II antagonists with non-.beta.-branched amino acids in position 5

AU Samanen, J.; Narindray, D.; Cash, T.; Brandeis, E.; Adams, W., Jr.; Yellin, T.; Eggleston, D.; DeBrosse, C.; Regoli, D.

CS Pept. Chem. Dep., Smith Kline and French Lab., Swedeland, PA, 19406-0939, USA

SO Journal of Medicinal Chemistry (1989), 32(2), 466-72

CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

OS CASREACT 110:58089

IT **117940-34-8P**

RL: SPN (Synthetic preparation); PREP (Preparation)

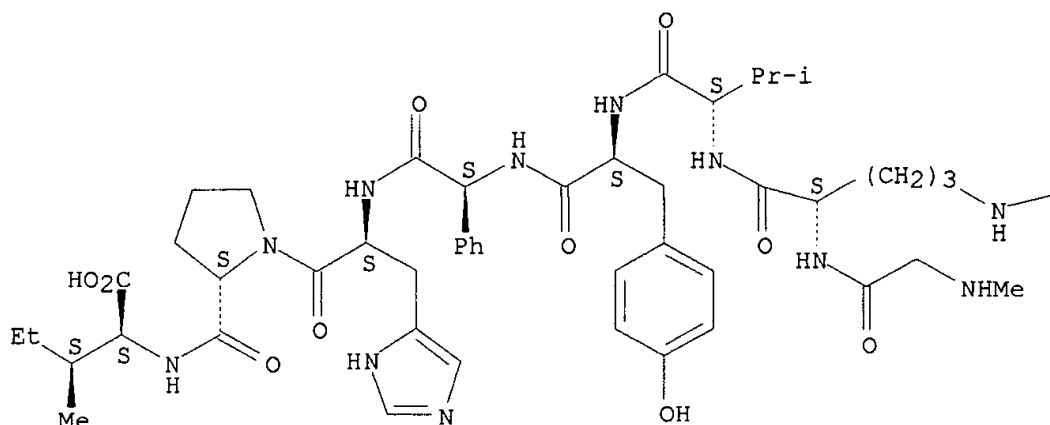
(prepn. and angiotensin II agonistic and antagonistic activities of)

RN 117940-34-8 CAPLUS

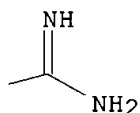
CN Angiotensin II, 1-(N-methylglycine)-5-(L-2-phenylglycine)-8-L-isoleucine-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



AB Amino acids with lipophilic side chains that contain more than one functional group on the .beta.-carbon, i.e. a .beta.-branched hydrocarbon moiety, are required in position 5 of angiotensin II (AII) analogs with potent agonist activity. This requirement for agonist activity does not follow for AII analogs with potent antagonist activity. Straight-chain amino acids may be substituted into position 5 of [Sar1,X5,Ile8]AII (Sar = sarcosine, X = amino acid) with retention or enhancement of antagonist activity. .beta.-Branched side chains can still enhance the antagonist activities of [Sar1,X5,Ile8]AII. An x-ray crystal structure of Me3CO2C-(.beta.Me)Phe-OH dicyclohexylamine salt, prepd. for the solid-phase synthesis of [Sar1,(.beta.Me)Phe5,Ile8]AII, revealed an S,S-configuration for the .alpha.- and .beta.-carbon atoms. Contrary to previous literature reports, chem. nonequivalence of the .delta.-protons of Pro was obsd. in the 1H NMR spectra of [Sar1,X5,Ile8]AII analogs bearing both .beta.-branched X5 side chains (X5 = Ile) and non-.beta.-branched X5 side chains (X5 = Ala, His).

L4 ANSWER 108 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1989:1065 CAPLUS

DN 110:1065

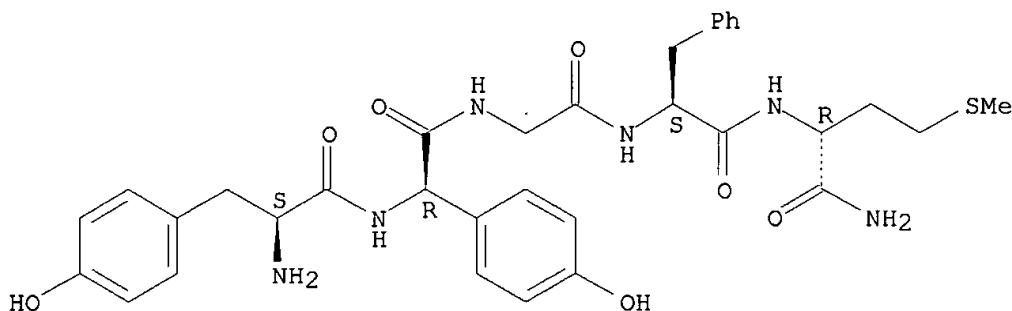
TI Synthesis and biological activity of analogs of leucine-/methionine-enkephalin

AU Sivanandaiah, K. M.; Gurusiddappa, S.; Palgunachari, M. N.

CS Cent. Coll., Bangalore Univ., Bangalore, 560 001, India

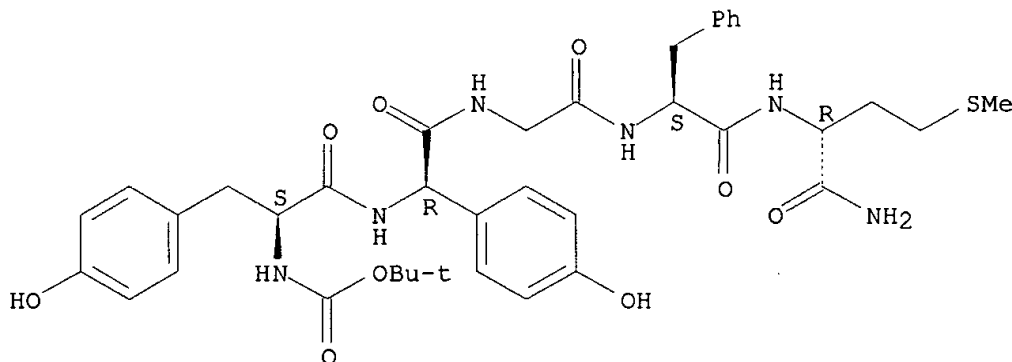
SO Indian Journal of Biochemistry & Biophysics (1988), 25(4), 356-9  
 CODEN: IJBBBQ; ISSN: 0301-1208  
 DT Journal  
 LA English  
 OS CASREACT 110:1065  
 IT **117747-75-8P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (prepn. and biol activity of, mol. structure in relation to)  
 RN 117747-75-8 CAPLUS  
 CN D-Methioninamide, L-tyrosyl-D-2-(4-hydroxyphenyl)glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



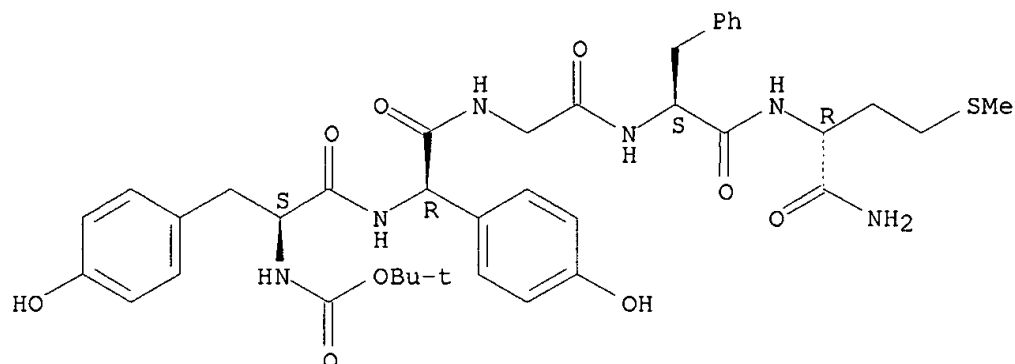
IT **117747-81-6DP**, polymer-bound **117747-81-6P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. and deprotection of)  
 RN 117747-81-6 CAPLUS  
 CN D-Methioninamide, N-[(1,1-dimethylethoxy)carbonyl]-L-tyrosyl-D-2-(4-hydroxyphenyl)glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 117747-81-6 CAPLUS  
 CN D-Methioninamide, N-[(1,1-dimethylethoxy)carbonyl]-L-tyrosyl-D-2-(4-hydroxyphenyl)glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Seven analogs of the opioid pentapeptides leucine- and methionine-enkephalinamides were synthesized by the solid-phase technique employing mainly 9-fluorenylmethyloxycarbonyl amino acid active esters in the presence of 1-hydroxybenzotriazole and the conventional chloromethylated copolystyrene-2% divinylbenzene (Merrifield) resin as the solid support. The analogs varied by replacing the amino acids at positions 2 and 5. Some of the analogs were highly potent in the guinea pig ileum assay. The analog Tyr-D-Met-Gly-Phe-D-Nva-NH<sub>2</sub> was the most potent analog of the series with analgesic and antidiarrheal activities of 0.6053 and 0.7129, resp., as compared to the ref. compd. morphine (1.0).

L4 ANSWER 109 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1988:132326 CAPLUS

DN 108:132326

TI Preparation of orally active luteinizing hormone-releasing hormone (LHRH) analogs

IN Almquist, Ronald G.; Olsen, Cris M.

PA SRI International, USA

SO U.S., 17 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
|    | -----      | ---- | -----    | -----           | -----    |
| PI | US 4705778 | A    | 19871110 | US 1985-790031  | 19851022 |
|    |            |      |          | US 1985-790031  | 19851022 |

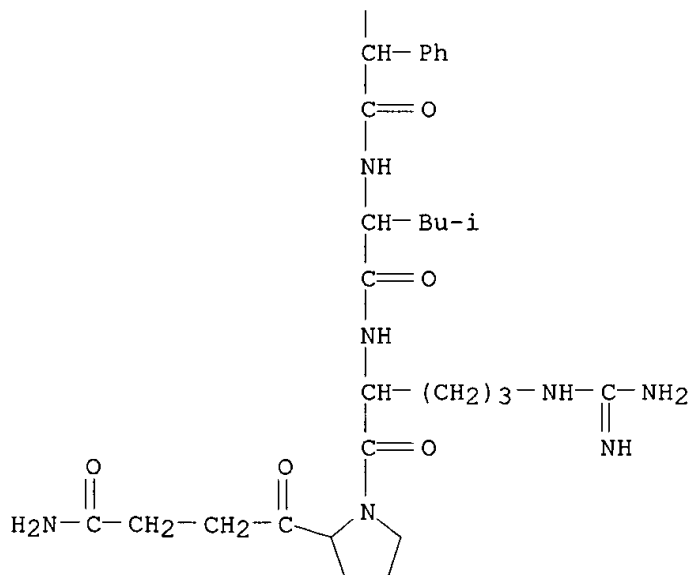
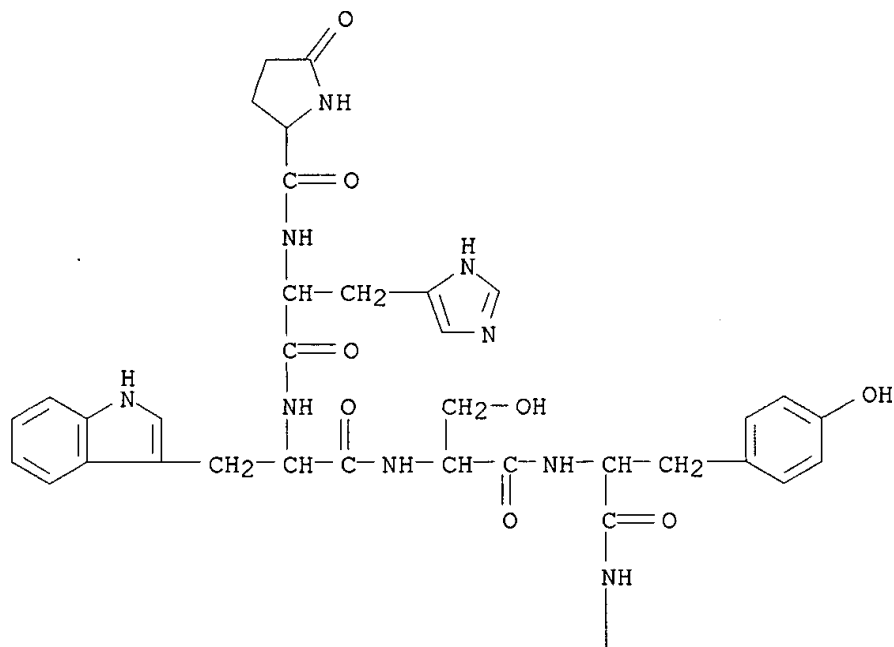
IT 113422-21-2P 113422-48-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as antitumor agent and contraceptive)

RN 113422-21-2 CAPLUS

CN Luteinizing hormone-releasing factor (swine), 6-(D-2-phenylglycine)-9-(.gamma.-oxo-2-pyrrolidinebutanamide)-10-deglycinamide-, (S)- (9CI) (CA INDEX NAME)



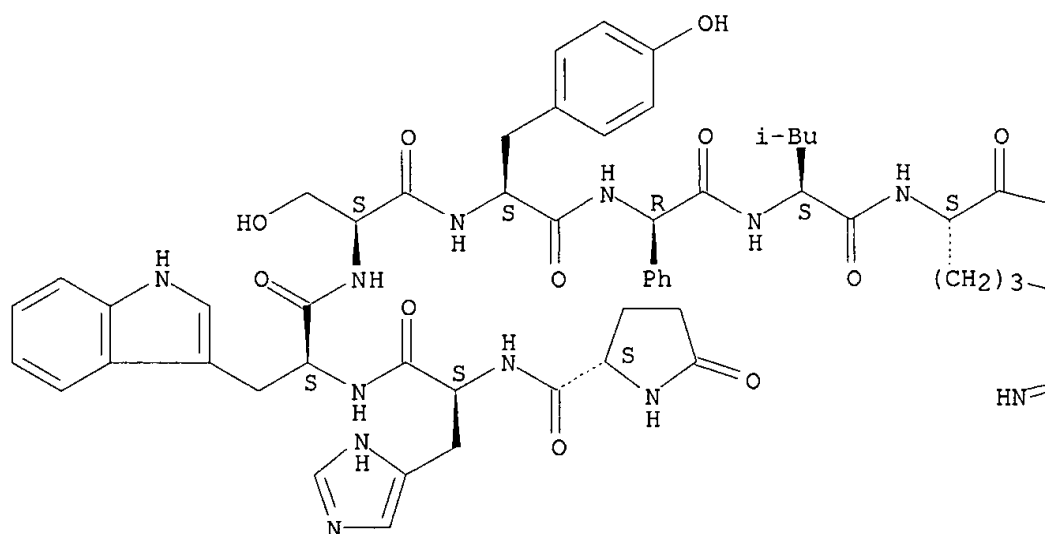


RN 113422-48-3 CAPLUS

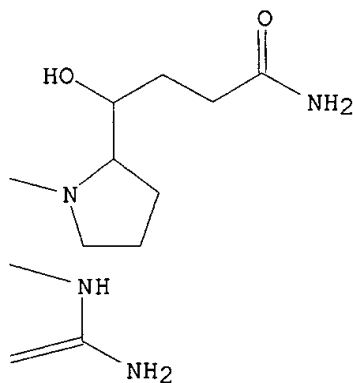
CN Luteinizing hormone-releasing factor (swine), 6-(D-2-phenylglycine)-9-( $\gamma$ -hydroxy-2-pyrrolidinebutanamide)-10-deglycinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



AB R1-R2-R3-Tyr-R4-R5-Arg-Pro-X-Gly-OH [I; R1 = H-pGlu, H-D-pGlu, Ac-D-Pro, Ac-Pro, Ac-Trp, Ac-D-Pr(halo-p), (un)substituted H-D-Ala, Ac-D-Phe, Ac-D-Phe(halo-p), D-Phe, D-Nal, or Ac-D-Nal, or (un)substituted H-Gly, H-D-Ala, H-ala, H-D-Trp, or H-D-Phe with benzoylalkanoyl, Bz, alkanoyl, acyl and HO<sub>2</sub>C(CH<sub>2</sub>)<sub>n</sub>CO (n = 2-6); R2 = His, Phe(halo), D-Phe(NO<sub>2</sub>), D-Phe(dihalo), (un)substituted D-Phe, Phe, (un)substituted D-Ala, diphenyl-Gly; R3 = Trp, D-Trp, Phe, (un)substituted D-Phe, substituted D-Ala, D-Nal; R4 = Gly, D-aminoacyl residue; R5 = Leu, MeLeu; X = COCH<sub>2</sub> or CH(OH)CH<sub>2</sub> replacing CONH linkage], useful as antitumor agents (no data) and male or female contraceptives, were prepd. [Ac-D-Phe<sub>1</sub>, D-Phe(Cl-p)<sub>2</sub>, D-Trp<sub>3</sub>, D-Arg<sub>6</sub>, Pro-COCH<sub>2</sub>Gly<sub>9,10</sub>]LHRH (II) was prepd. by the solid phase method using BOC-Pro-COCH<sub>2</sub>Gly-OH coupled to a benzhydrylaminopolystyrene-

2% divinylbenzene resin. The antioviulatory activity of II in rats was more than twice that of its regular amide-bonded counterpart (III).

L4 ANSWER 110 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1988:38432 CAPLUS

DN 108:38432

TI Preparation of renin-inhibiting peptides for treatment of hypertension and cardiac insufficiency

IN Breipohl, Gerhard; Knolle, Jochen; Wegmann, Helmut; Ruppert, Dieter

PA Hoechst A.-G. , Fed. Rep. Ger.

SO Ger. Offen., 22 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | DE 3601248  | A1   | 19870723 | DE 1986-3601248 | 19860117 |
|    | EP 230242   | A2   | 19870729 | EP 1987-100275  | 19870112 |
|    | EP 230242   | A3   | 19900117 |                 |          |
|    | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                 |          |
|    | DK 8700236  | A    | 19870718 | DK 1987-236     | 19870116 |
|    |   |      |          | DE 1986-3601248 | 19860117 |
|    | JP 62265263   | A2   | 19871118 | JP 1987-6308    | 19870116 |
|    |   |      |          | DE 1986-3601248 | 19860117 |

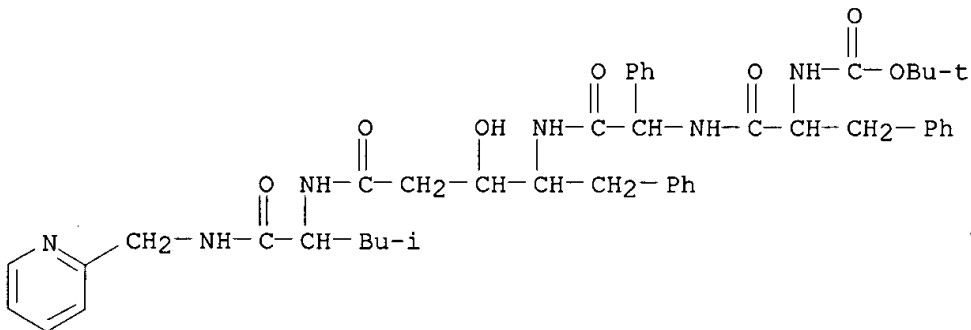
OS CASREACT 108:38432

IT **110695-52-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. of, as antihypertensive)

RN 110695-52-8 CAPLUS

CN L-threo-Pentonamide, 2,4,5-trideoxy-4-[[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl]-L-2-phenylglycyl]amino]-N-[3-methyl-1-[(2-pyridinylmethyl)amino]carbonyl]butyl]-5-phenyl-, (S)- (9CI)  
(CA INDEX NAME)



AB The title compds. R1ABNHCHR2CHOHCHR3COR4 [I; R1 = null, H, (substituted) alkyl, acyl; R2 = H, (substituted) alkyl, alkylcycloalkyl, aralkyl, aryl; R3 = H, (substituted) alkyl; R4 = amino; A, B = amino acid residue] were prepd. as antihypertensives (no data). BOC-Phe-His(DNP)-OH (BOC =

tert-butoxycarbonyl, DNP = 2,4-dinitrophenyl) and H-Sta-Leu-Asn-NH<sub>2</sub> [Sta = [3S,4S]-4-amino-3-hydroxy-6-methylheptanoic acid residue] were coupled using dicyclohexylcarbodiimide and 1-hydroxybenzotriazole. The resulting peptide was treated with thiophenol in DMF to give BOC-Phe-His-Sta-Leu-Asn-NH<sub>2</sub>.

L4 ANSWER 111 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1988:22252 CAPLUS

DN 108:22252

TI Syntheses and biological activities of neurokinin B analogs modified at positions 2, 3, and 6

AU Uchida, Yoshiki; Okimura, Keiko; Kurosawa, Katsuro; Sakura, Naoki; Hirose, Kyoko; Hashimoto, Tadashi

CS Sch. Pharm., Hokuriku Univ., Kanazawa, 920-11, Japan

SO Bulletin of the Chemical Society of Japan (1987), 60(4), 1561-3

CODEN: BCSJA8; ISSN: 0009-2673

DT Journal

LA English

IT 111895-96-6P

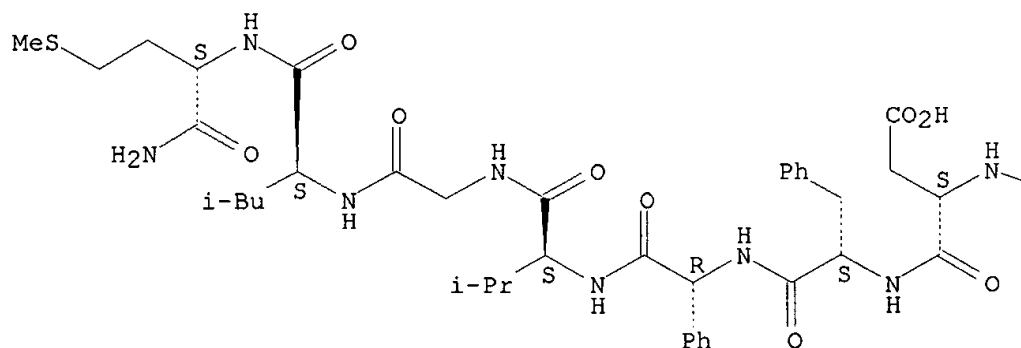
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 111895-96-6 CAPLUS

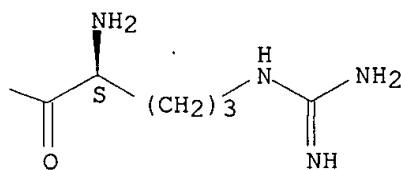
CN L-Methioninamide, L-arginyl-L-.alpha.-aspartyl-L-phenylalanyl-D-2-phenylglycyl-L-valylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



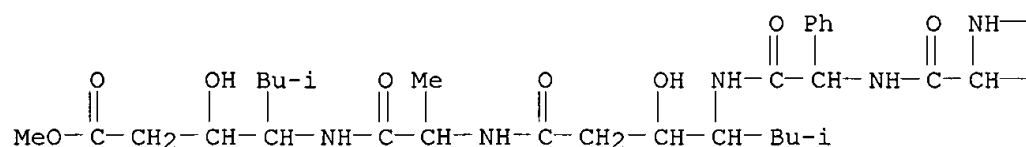
PAGE 1-B



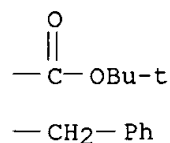
AB Title analogs H-His-Asp-Phe-X-X1-Gly-Leu-Met-NH<sub>2</sub> (X-X1 = Gly-Val, Phe-Gly), H-Arg-Asp-Phe-X-Val-Gly-Leu-Met-NH<sub>2</sub> (I; X = MeGly, D-Ala, D-Phe, D-Trp, D-2-phenylglycine residue), and H-Arg-His-Asp-Phe-X-Val-Gly-Leu-Met-NH<sub>2</sub> (X = D-Arg, D-Pro, D-homoglutamine residue, D-homoglutamic acid residue) were prepd. by the solid-phase method. The biol. activity of the above peptides were assayed on isolated guinea pig ileum. I (D-Ala) acts as an antagonist of neurokinin B.

L4 ANSWER 112 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1987:593937 CAPLUS  
 DN 107:193937  
 TI Renin inhibitors. Free-Wilson and correlation analysis of the inhibitory potency of a series of pepstatin analogs on plasma renin  
 AU Nisato, Dino; Wagnon, Jean; Callet, Georges; Mettefeu, Daniel; Assens, Jean Louis; Plouzane, Claude; Tonnerre, Bernard; Pliska, Vladimir; Fauchere, Jean Luc  
 CS SANOFI Rech., Montpellier, F-34082, Fr.  
 SO Journal of Medicinal Chemistry (1987), 30(12), 2287-91  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DT Journal  
 LA English  
 IT **105382-21-6**  
 RL: BIOL (Biological study)  
 (renin inhibition by, Free-Wilson and correlation anal. of)  
 RN 105382-21-6 CAPLUS  
 CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[2-hydroxy-4-[[2-[[2-hydroxy-4-methoxy-1-(2-methylpropyl)-4-oxobutyl]amino]-1-methyl-2-oxoethyl]amino]-1-(2-methylpropyl)-4-oxobutyl]-L-2-phenyl-, stereoisomer (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



AB Free-Wilson and correlation anal. were combined to study a series of 34 pepstatin analogs in which mainly position 2 was varied. A statistically highly significant correlation was found between the inhibitory activity of the analogs on an enriched plasma renin prepn. and structural parameters of the amino acid side chain in position 2. The crucial parameters were found to be the NMR chem. shift of the .alpha.-C, the localized elec. (inductive) effect, and the van der Waals radius-related

steric parameter, which demonstrated the dominating influence of electronic inductive effects compared to steric bulk. The model gives insight into the structural requirements for effective inhibition and suggests the histidine-2 deriv., a pos. outlier in this series, as a lead compd. for further structure-activity studies.

L4 ANSWER 113 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1987:554732 CAPLUS

DN 107:154732

TI Solid phase synthesis of substance P and its analogs employing 9-fluorenylmethoxycarbonyl amino acid active esters

AU Sivanandaiah, K. M.; Rangaraju, N. S.

CS Cent. Coll., Bangalore Univ., Bangalore, 560 001, India

SO Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1986), 25B(10), 1045-9

CODEN: IJSBDB; ISSN: 0376-4699

DT Journal

LA English

OS CASREACT 107:154732

IT **110449-80-4P**

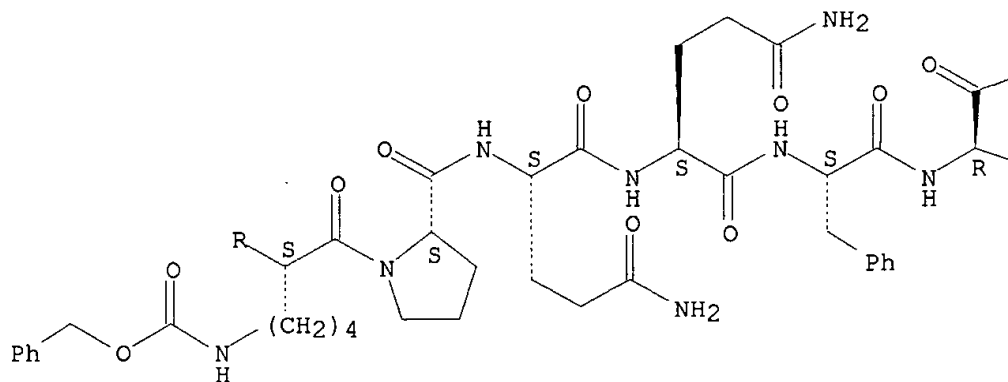
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and deblocking of)

RN 110449-80-4 CAPLUS

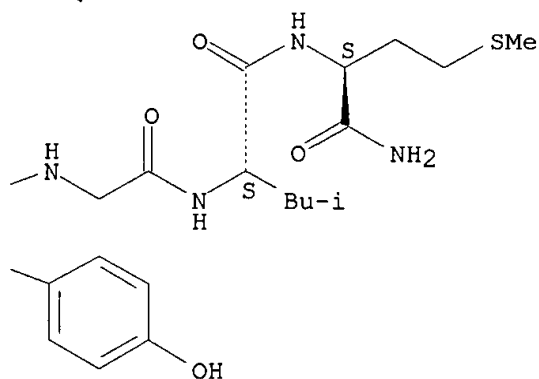
CN Substance P, 1-[N5-[imino(nitroamino)methyl]-N2-[(phenylmethoxy)carbonyl]-L-ornithine]-3-[N6-[(phenylmethoxy)carbonyl]-L-lysine]-8-[D-2-(4-hydroxyphenyl)glycine]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

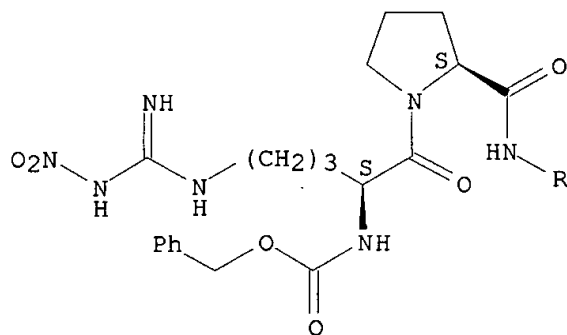
PAGE 1-A



PAGE 1-B



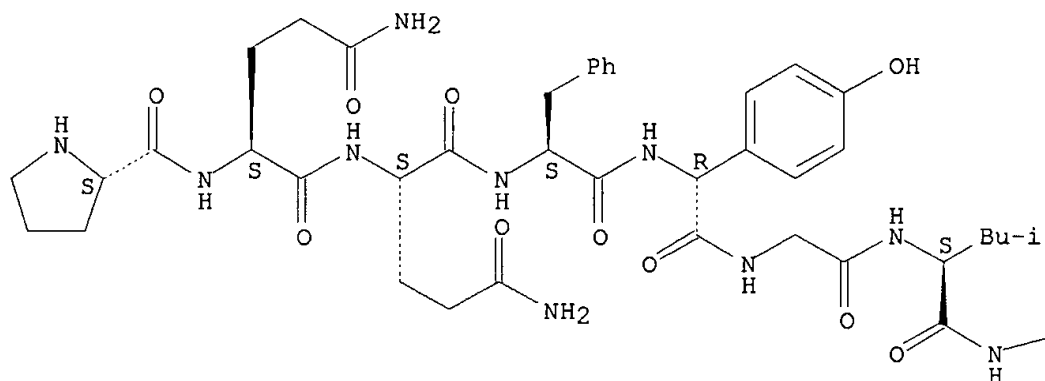
PAGE 2-A



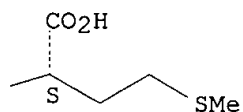
IT **110449-68-8DP**, p-alkoxybenzyl alc. resin-bound  
**110449-71-3DP**, p-alkoxybenzyl alc. resin-bound  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and resin cleavage of, by ammonolysis)  
 RN 110449-68-8 CAPLUS  
 CN Substance P, 1-de-L-arginine-2-de-L-proline-3-de-L-lysine-8-[D-2-(4-hydroxyphenyl)glycine]-11-L-methionine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



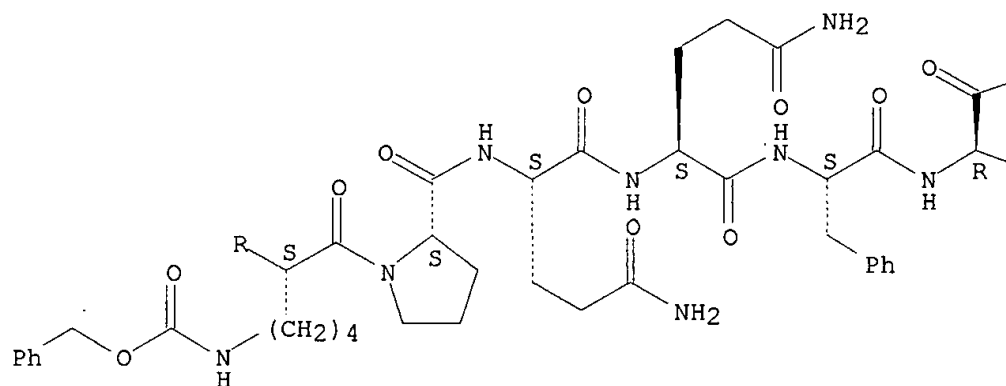
RN 110449-71-3 CAPLUS

CN Substance P, 1-[N5-[imino(nitroamino)methyl]-N2-[(phenylmethoxy)carbonyl]-L-ornithine]-3-[N6-[(phenylmethoxy)carbonyl]-L-lysine]-8-[D-2-(4-hydroxyphenyl)glycine]-11-L-methionine- (9CI) (CA INDEX NAME)

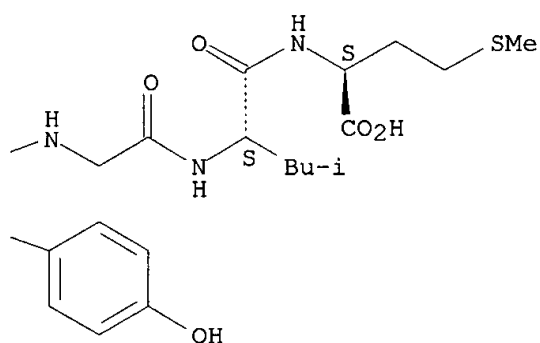
Absolute stereochemistry.



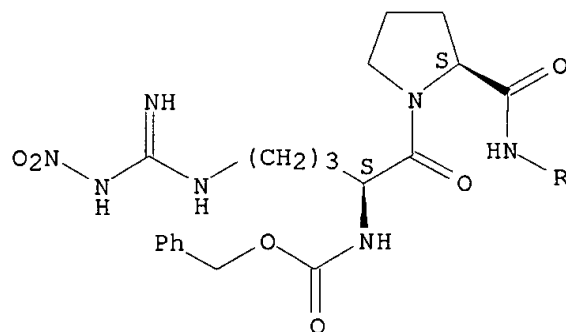
PAGE 1-A



PAGE 1-B



PAGE 2-A



IT 110449-76-8P 110465-51-5P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, by solid-phase method on alkoxybenzyl alc. resin)

RN 110449-76-8 CAPLUS

CN Substance P, 1-de-L-arginine-2-de-L-proline-3-de-L-lysine-8-[D-2-(4-hydroxyphenyl)glycine]-, monoacetate (salt) (9CI) (CA INDEX NAME)

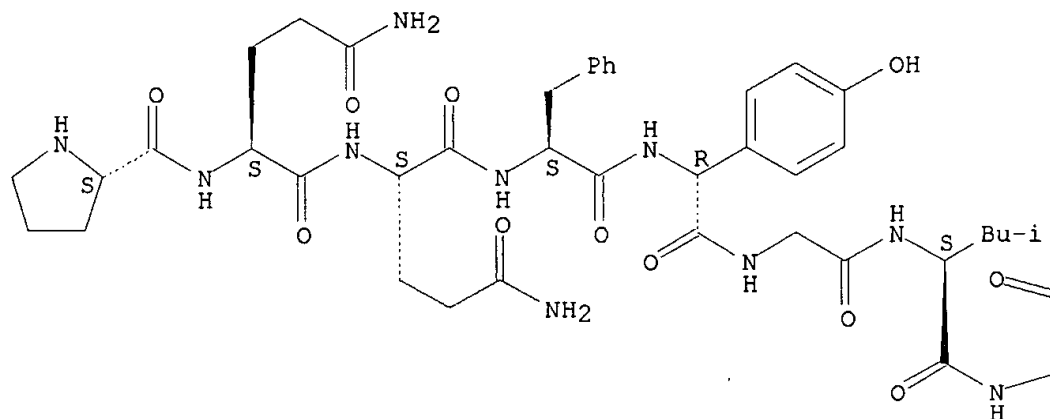
CM 1

CRN 110449-75-7

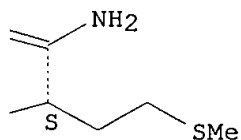
CMF C45 H65 N11 O11 S

Absolute stereochemistry.

PAGE 1-A



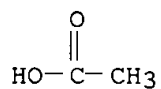
PAGE 1-B



CM 2

CRN 64-19-7

CMF C2 H4 O2



RN 110465-51-5 CAPLUS

CN Substance P, 8-[D-2-(4-hydroxyphenyl)glycine]-, triacetate (salt) (9CI)  
(CA INDEX NAME)

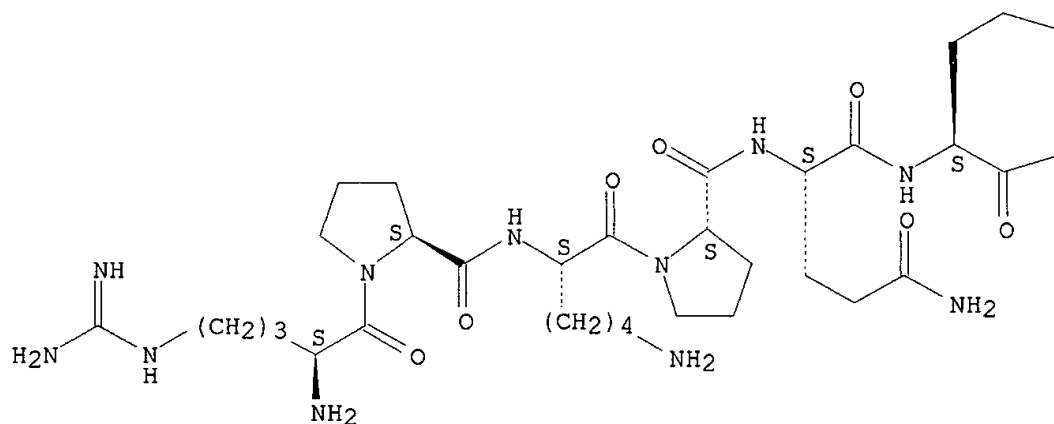
CM 1

CRN 110465-50-4

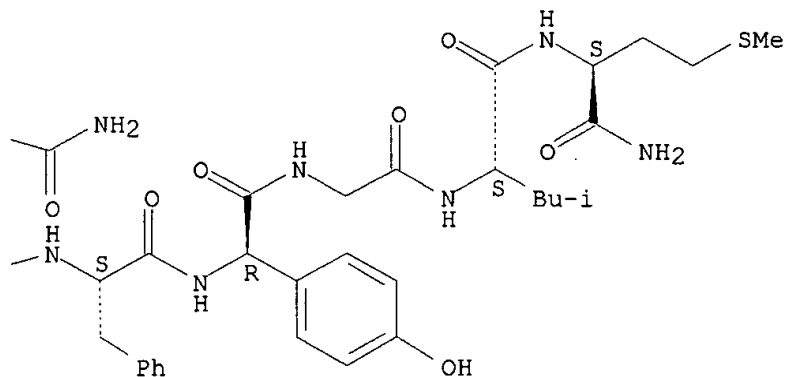
CMF C62 H96 N18 O14 S

Absolute stereochemistry.

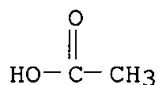
PAGE 1-A



PAGE 1-B



CM 2

CRN 64-19-7  
CMF C2 H4 O2

AB Substance P, H-Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH<sub>2</sub>, and analogs H-Pro-Gln-Gln-X-X<sub>1</sub>-Gly-Leu-Met-NH<sub>2</sub> [X-X<sub>1</sub> = D-Phg(4-OH)-Phe [Phg(4-OH) = NHCH(C<sub>6</sub>H<sub>4</sub>OH-4)CO], Phe-D-Phg(4-OH), D-Phg(4-OH)-D-Phg(4-OH)] and H-Arg-Pro-Lys-Pro-Gln-Gln-X-X<sub>1</sub>-Gly-Leu-Met-NH<sub>2</sub> (X-X<sub>1</sub> = same) were prepd. by the solid-phase method on p-alkoxybenzyl alc. resin using 9-fluorenylmethoxycarbonyl (Fmoc) amino acid trichlorophenyl active esters in the presence of 1-hydroxybenzotriazole. The Fmoc groups were cleaved by Et<sub>2</sub>NH. Agonistic and antagonistic activities of the peptides were studied.

L4 ANSWER 114 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1986:627342 CAPLUS

DN 105:227342

TI Pepstatin analogs

IN Wagnon, Jean le Hameau de la Rauze; Callet, Georges; Gagnol, Jean Pierre; Nisato, Dino; Cazaubon, Catherine

PA SANOFI, Fr.; Institut National de la Sante et de la Recherche Medicale (INSERM)

SO Eur. Pat. Appl., 38 pp.

CODEN: EPXXDW

DT Patent

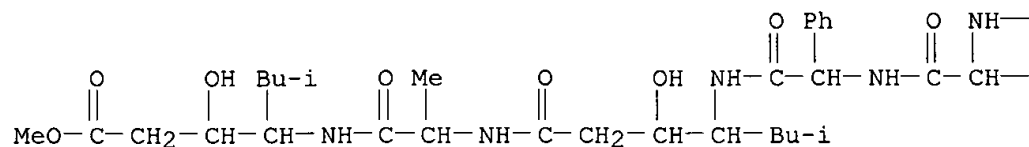
LA French

FAN.CNT 1

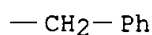
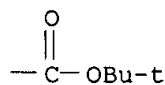
|    | PATENT NO.                                    | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 192554                                     | A1   | 19860827 | EP 1986-400271  | 19860210 |
|    | EP 192554                                     | B1   | 19920102 |                 |          |
|    | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE |      |          |                 |          |
|    |   |      |          | FR 1985-1981    | 19850212 |
|    |   |      |          | FR 1985-1982    | 19850212 |
|    | FR 2577225                                    | A1   | 19860814 | FR 1985-1981    | 19850212 |
|    | FR 2577225                                    | B1   | 19870828 |                 |          |
|    | FR 2577226                                    | A1   | 19860814 | FR 1985-1982    | 19850212 |
|    | FR 2577226                                    | B1   | 19900615 |                 |          |
|    | CA 1286846                                    | A1   | 19910723 | CA 1986-500927  | 19860203 |
|    |   |      |          | FR 1985-1981    | 19850212 |
|    |   |      |          | FR 1985-1982    | 19850212 |
|    | US 4725580                                    | A    | 19880216 | US 1986-826349  | 19860205 |
|    |   |      |          | FR 1985-1981    | 19850212 |
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|    | US 4746648                                    | A    | 19880524 | US 1986-826375  | 19860205 |
|    |   |      |          | FR 1985-1981    | 19850212 |
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|    |   |      |          | FR 1985-1981    | 19850212 |

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|-------------|----|--|---|----------|
| AU 8653272  | A1 | 19860814   | FR 1985-1982                                  | 19850212 |
| AU 606312   | B2 | 19910207   | AU 1986-53272                                 | 19860206 |
|             |    |  | FR 1985-1981                                  | 19850212 |
| AU 8653273  | A1 | 19860821   | FR 1985-1982                                  | 19850212 |
| AU 606572   | B2 | 19910214   | AU 1986-53273                                 | 19860206 |
|             |    |  | FR 1985-1981                                  | 19850212 |
| DK 8600640  | A  | 19860813   | FR 1985-1982                                  | 19850212 |
|             |    |  | DK 1986-640                                   | 19860210 |
|             |    |  | FR 1985-1981                                  | 19850212 |
| DK 8600641  | A  | 19860813   | FR 1985-1982                                  | 19850212 |
|             |    |  | DK 1986-641                                   | 19860210 |
|             |    |  | FR 1985-1981                                  | 19850212 |
| EP 193445   | A1 | 19860903   | FR 1985-1982                                  | 19850212 |
| EP 193445   | B1 | 19900509   | EP 1986-400272                                | 19860210 |
|             |    |  | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE |          |
|             |    |  | FR 1985-1981                                  | 19850212 |
| ZA 8600960  | A  | 19861029   | FR 1985-1982                                  | 19850212 |
|             |    |  | ZA 1986-960                                   | 19860210 |
| ZA 8600961  | A  | 19861029   | FR 1985-1981                                  | 19850212 |
|             |    |  | ZA 1986-961                                   | 19860210 |
| AT 52518    | E  | 19900515   | FR 1985-1981                                  | 19850212 |
|             |    |  | AT 1986-400272                                | 19860210 |
|             |    |  | FR 1985-1981                                  | 19850212 |
|             |    |  | FR 1985-1982                                  | 19850212 |
| AT 71111    | E  | 19920115   | EP 1986-400272                                | 19860210 |
|             |    |  | AT 1986-400271                                | 19860210 |
|             |    |  | FR 1985-1981                                  | 19850212 |
|             |    |  | FR 1985-1982                                  | 19850212 |
| ES 551820   | A1 | 19861216   | EP 1986-400271                                | 19860210 |
|             |    |  | ES 1986-551820                                | 19860211 |
|             |    |  | FR 1985-1981                                  | 19850212 |
| ES 551821   | A1 | 19870101   | FR 1985-1982                                  | 19850212 |
|             |    |  | ES 1986-551821                                | 19860211 |
|             |    |  | FR 1985-1981                                  | 19850212 |
| JP 61186397 | A2 | 19860820   | FR 1985-1982                                  | 19850212 |
|             |    |  | JP 1986-28747                                 | 19860212 |
|             |    |  | FR 1985-1981                                  | 19850212 |
| JP 61186398 | A2 | 19860820   | FR 1985-1982                                  | 19850212 |
|             |    |  | JP 1986-28748                                 | 19860212 |
|             |    |  | FR 1985-1981                                  | 19850212 |
|             |    |  | FR 1985-1982                                  | 19850212 |
| OS          |    | CASREACT 105:227342  |   |          |
| IT          |    | <b>105382-21-6P</b>  |   |          |
|             |    | RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  |   |          |
|             |    | (prepn. of, as renin inhibitor)  |   |          |
| RN          |    | 105382-21-6 CAPLUS   |   |          |
| CN          |    | Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[2-hydroxy-4-[[2-[[2-hydroxy-4-methoxy-1-(2-methylpropyl)-4-oxobutyl]amino]-1-methyl-2-oxoethyl]amino]-1-(2-methylpropyl)-4-oxobutyl]-L-2-phenyl-, stereoisomer (9CI) (CA INDEX NAME) |   |          |

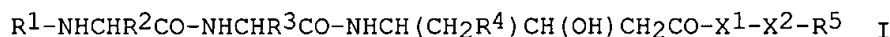
PAGE 1-A



PAGE 1-B



GI



AB Title peptides I (R1 = alkanoyl, arylcarbonyl, carbalkoxy, etc.; R2 = alkyl, phenylalkyl, naphthylalkyl, pyridylalkyl, etc.; R3 = H, alkenyl, Ph, naphthyl, etc.; R4 = CHMe2, Ph, cyclohexyl; R5 = OH, alkoxy, NH2, etc.; X1X2 = Ala-Sta, Ala-Leu, Leu-Phe, Val-Sta, etc.) (Sta = statine) were prepd., and they exhibited renin-inhibiting activity. Thus, BOC-Phe-Asp(CH2Ph)-Sta-Ala-Leu-OMe was prepd. by soln. method peptide synthesis.

L4 ANSWER 115 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1986:514756 CAPLUS

DN 105:114756

TI Anilide derivatives of substituted arylacetic acids

IN Kawakami, Hajime; Hashimoto, Katsuhiko; Tamoto, Katsumi; Ono, Keiichi; Yamamoto, Michihiro

PA Sumitomo Pharmaceuticals Co., Ltd., Japan

SO Eur. Pat. Appl., 28 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.                                | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 184822                                 | A2   | 19860618 | EP 1985-115720  | 19851210 |
|    | EP 184822                                 | A3   | 19871209 |                 |          |
|    | R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE |      |          |                 |          |
|    |   |      |          | JP 1984-261197  | 19841211 |
|    | JP 61140556                               | A2   | 19860627 | JP 1984-261197  | 19841211 |
|    | AU 8551065                                | A1   | 19860619 | AU 1985-51065   | 19851210 |
|    |   |      |          | JP 1984-261197  | 19841211 |
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|    |   |      |          | JP 1984-261197  | 19841211 |

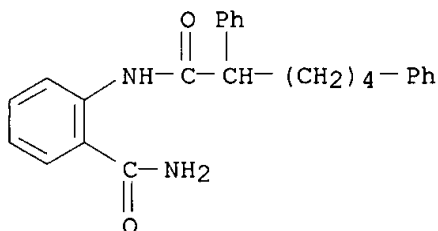
OS CASREACT 105:114756

IT **104122-31-8P 104122-32-9P 104122-33-0P**  
**104122-34-1P 104122-35-2P 104122-36-3P**  
**104122-37-4P 104122-38-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, as nootropic and cerebral metabolic stimulant)

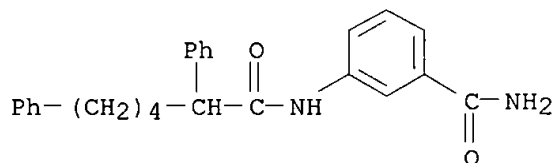
RN 104122-31-8 CAPLUS

CN Benzenhexanamide, N-[2-(aminocarbonyl)phenyl]-.alpha.-phenyl- (9CI) (CA  
 INDEX NAME)



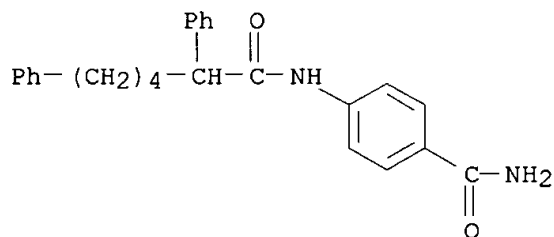
RN 104122-32-9 CAPLUS

CN Benzenhexanamide, N-[3-(aminocarbonyl)phenyl]-.alpha.-phenyl- (9CI) (CA  
 INDEX NAME)



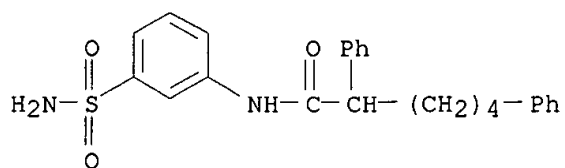
RN 104122-33-0 CAPLUS

CN Benzenhexanamide, N-[4-(aminocarbonyl)phenyl]-.alpha.-phenyl- (9CI) (CA  
 INDEX NAME)



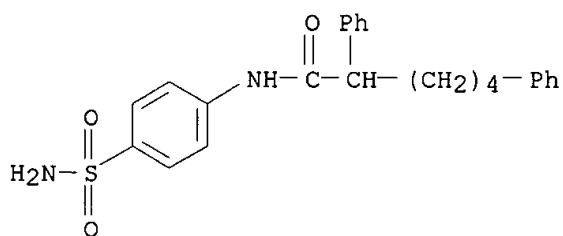
RN 104122-34-1 CAPLUS

CN Benzenhexanamide, N-[3-(aminosulfonyl)phenyl]-.alpha.-phenyl- (9CI) (CA  
 INDEX NAME)



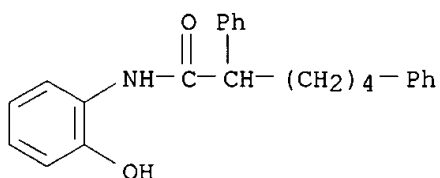
RN 104122-35-2 CAPLUS

CN Benzenhexanamide, N-[4-(aminosulfonyl)phenyl]-.alpha.-phenyl- (9CI) (CA INDEX NAME)



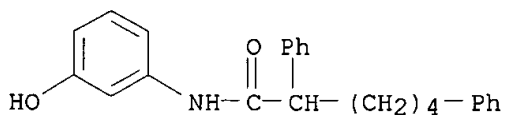
RN 104122-36-3 CAPLUS

CN Benzenhexanamide, N-(2-hydroxyphenyl)-.alpha.-phenyl- (9CI) (CA INDEX NAME)



RN 104122-37-4 CAPLUS

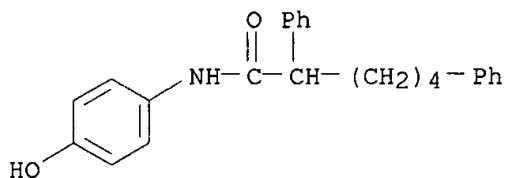
CN Benzenhexanamide, N-(3-hydroxyphenyl)-.alpha.-phenyl- (9CI) (CA INDEX NAME)



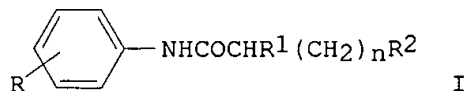
RN 104122-38-5 CAPLUS

CN Benzenhexanamide, N-(4-hydroxyphenyl)-.alpha.-phenyl- (9CI) (CA INDEX NAME)





GI



I

AB Arylacetanilides I [R = OH, CONR<sub>3</sub>R<sub>4</sub>, SO<sub>2</sub>NR<sub>3</sub>R<sub>4</sub>; R<sub>1</sub> = (un)substituted heterocyclyl, arom. hydrocarbyl; R<sub>2</sub> = heterocyclyl, arom. hydrocarbyl; R<sub>3</sub>, R<sub>4</sub> = H, alkyl; NR<sub>3</sub>R<sub>4</sub> = pyrrolidino, piperidino, morpholino, N-alkyl- or N-phenylpiperazino; n = 1-4] are prepd. (50 examples) as nootropics and cerebral metabolic stimulants. Thus, PhCH<sub>2</sub>CHPhCO<sub>2</sub>H was refluxed with SOCl<sub>2</sub>, the mixt. distd., and the residue dissolved in THF and added to 3-H<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CONH<sub>2</sub> and Et<sub>3</sub>N in THF to give I (R = 3-CONH<sub>2</sub>, R<sub>1</sub> = R<sub>2</sub> = Ph, n = 1) (II). Whereas the survival times of hypoxic mice were effectively extended (to >140 s) by bencyclane, papaverine, and vincamine at 30 mg/kg, only 10 mg II/kg was required.

L4 ANSWER 116 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1986:435745 CAPLUS

DN 105:35745

TI Synthesis and biological activity of some new leucine-enkephalin analogs

AU Sivanandaiah, K. M.; Gurusiddappa, S.; Rangaraju, N. S.

CS Cent. Coll., Bangalore Univ., Bangalore, 560 001, India

SO Journal of Biosciences (Bangalore, India) (1985), 8(1-2), 263-71

CODEN: JOBSDN; ISSN: 0250-4774

DT Journal

LA English

IT 103144-89-4DP, resin complexes

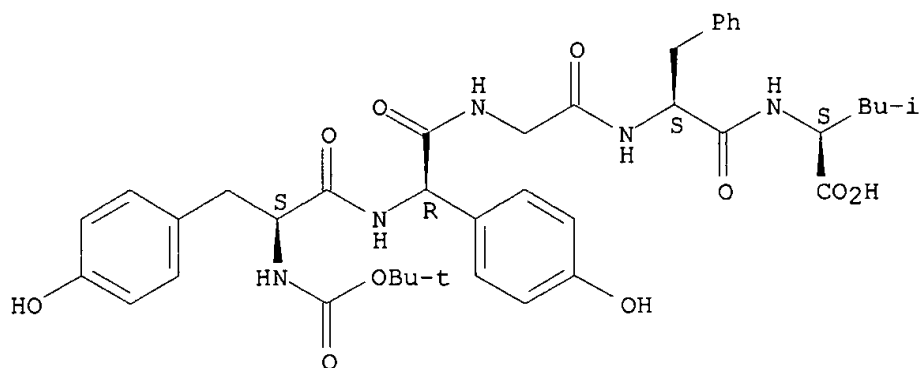
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and aminolysis of)

RN 103144-89-4 CAPLUS

CN L-Leucine, N-[N-[N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-tyrosyl]-D-2-(4-hydroxyphenyl)glycyl]glycyl]-L-phenylalanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



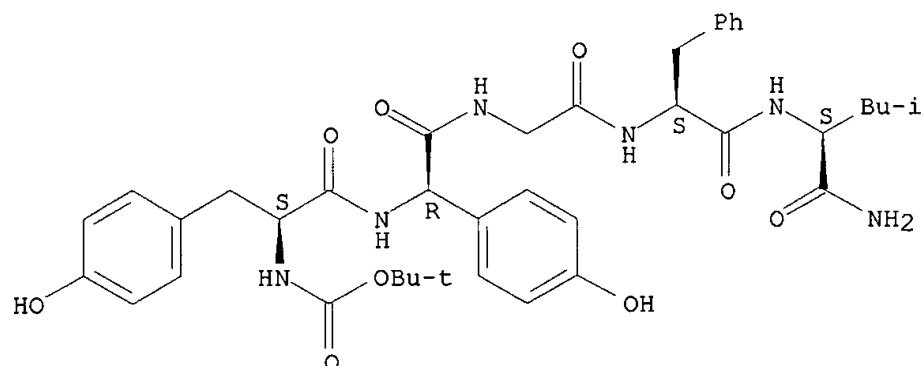
IT **103144-99-6P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and deprotection of)

RN 103144-99-6 CAPLUS

CN L-Leucinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-tyrosyl-D-2-(4-hydroxyphenyl)glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



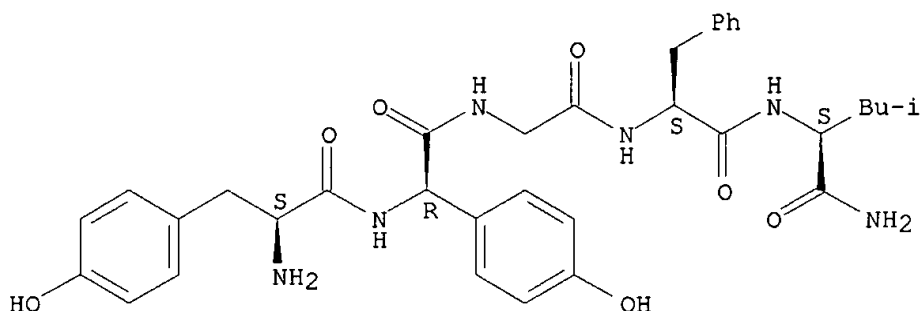
IT **103175-20-8P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and muscle contraction inhibition by)

RN 103175-20-8 CAPLUS

CN L-Leucinamide, L-tyrosyl-D-2-(4-hydroxyphenyl)glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The opioid pentapeptide leucine-enkephalinamide and 11 of its analogs were synthesized by the solid-phase technique employing mostly 9-fluorenylmethoxycarbonyl amino acid active esters in the presence of 1-hydroxybenzotriazole. Both the conventional chloromethylated copolystyrene-2% divinylbenzene resin as well as p-alkoxybenzyl alc. resin were employed and yields were uniformly better with the latter resin. The analogs were made by affecting single or multiple replacements of amino acids involving positions 1, 2, and 5. Some of the analogs were more potent than morphine in inhibiting elec. induced contraction in the guinea pig ileum assay.

L4 ANSWER 117 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1984:591513 CAPLUS

DN 101:191513

TI Cephalosporin derivatives, and prophylactic and therapeutic agents for bacterial infection

IN Kakeya, Nobuharu; Nishizawa, Susumu; Tamaki, Satoshi; Kitao, Kazuhiko

PA Kyoto Pharmaceutical Industries, Ltd., Japan

SO Eur. Pat. Appl., 84 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 2

|    | PATENT NO.                                | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 108942                                 | A2   | 19840523 | EP 1983-110284  | 19831015 |
|    | EP 108942                                 | A3   | 19850515 |                 |          |
|    | EP 108942                                 | B1   | 19880302 |                 |          |
|    | R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE |      |          |                 |          |
|    | WO 8401949                                | A1   | 19840524 | WO 1982-JP437   | 19821110 |
|    | W: MC                                     |      |          | WO 1982-JP437   | 19821110 |
|    | US 4605651                                | A    | 19860812 | US 1983-540676  | 19831011 |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | ZA 8307635                                | A    | 19841128 | ZA 1983-7635    | 19831013 |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | AU 8320199                                | A1   | 19840517 | AU 1983-20199   | 19831014 |
|    | AU 568094                                 | B2   | 19871217 |                 |          |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    | AT 32724                                  | E    | 19880315 | AT 1983-110284  | 19831015 |
|    |   |      |          | WO 1982-JP437   | 19821110 |
|    |   |      |          | EP 1983-110284  | 19831015 |
|    | NO 8303807                                | A    | 19840511 | NO 1983-3807    | 19831019 |
|    | NO 162240                                 | B    | 19890821 |                 |          |

|             |    |          |
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| NO 162240   | C  | 19891129 |
| ES 526561   | A1 | 19850416 |
| SU 1331432  | A3 | 19870815 |
| FI 8303839  | A  | 19840511 |
| FI 75348    | B  | 19880229 |
| FI 75348    | C  | 19880609 |
| DK 8304818  | A  | 19840511 |
| JP 59116292 | A2 | 19840705 |
| CA 1239928  | A1 | 19880802 |
| ES 532996   | A1 | 19850816 |
| ES 532997   | A1 | 19850816 |
| SU 1322983  | A3 | 19870707 |

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| WO 1982-JP437   | 19821110 |
| ES 1983-526561  | 19831019 |
| WO 1982-JP437   | 19821110 |
| SU 1983-3655401 | 19831019 |
| WO 1982-JP437   | 19821110 |
| FI 1983-3839    | 19831020 |
| WO 1982-JP437   | 19821110 |
| DK 1983-4818    | 19831020 |
| WO 1982-JP437   | 19821110 |
| JP 1983-197458  | 19831020 |
| WO 1982-JP437   | 19821110 |
| CA 1983-439358  | 19831020 |
| WO 1982-JP437   | 19821110 |
| ES 1984-532996  | 19840531 |
| WO 1982-JP437   | 19821110 |
| ES 1984-532997  | 19840531 |
| WO 1982-JP437   | 19821110 |
| SU 1984-3827995 | 19841224 |
| WO 1982-JP437   | 19821110 |

## PATENT FAMILY INFORMATION:

FAN 1987:636362

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|-------------|------|----------|-----------------|----------|
| PI | SU 1309912  | A3   | 19870507 | SU 1984-3826171 | 19841224 |
|    | WO 8401949  | A1   | 19840524 | WO 1982-JP437   | 19821110 |
|    | W: MC       |      |          | WO 1982-JP437   | 19821110 |
|    | US 4605651  | A    | 19860812 | US 1983-540676  | 19831011 |
|    | ZA 8307635  | A    | 19841128 | WO 1982-JP437   | 19821110 |
|    | AU 8320199  | A1   | 19840517 | ZA 1983-7635    | 19831013 |
|    | AU 568094   | B2   | 19871217 | WO 1982-JP437   | 19821110 |
|    | NO 8303807  | A    | 19840511 | AU 1983-20199   | 19831014 |
|    | NO 162240   | B    | 19890821 | WO 1982-JP437   | 19821110 |
|    | NO 162240   | C    | 19891129 | NO 1983-3807    | 19831019 |
|    | ES 526561   | A1   | 19850416 | WO 1982-JP437   | 19821110 |
|    | SU 1331432  | A3   | 19870815 | ES 1983-526561  | 19831019 |
|    | FI 8303839  | A    | 19840511 | WO 1982-JP437   | 19821110 |
|    | FI 75348    | B    | 19880229 | SU 1983-3655401 | 19831019 |
|    | FI 75348    | C    | 19880609 | WO 1982-JP437   | 19821110 |
|    | DK 8304818  | A    | 19840511 | FI 1983-3839    | 19831020 |
|    | JP 59116292 | A2   | 19840705 | WO 1982-JP437   | 19821110 |
|    | CA 1239928  | A1   | 19880802 | DK 1983-4818    | 19831020 |
|    | ES 532996   | A1   | 19850816 | WO 1982-JP437   | 19821110 |
|    |             |      |          | JP 1983-197458  | 19831020 |
|    |             |      |          | WO 1982-JP437   | 19821110 |
|    |             |      |          | CA 1983-439358  | 19831020 |
|    |             |      |          | WO 1982-JP437   | 19821110 |
|    |             |      |          | ES 1984-532996  | 19840531 |
|    |             |      |          | WO 1982-JP437   | 19821110 |

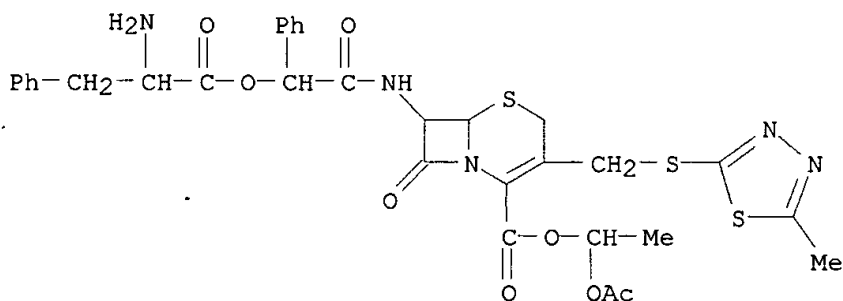
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|------------|----|----------|-----------------|----------|
| ES 532997  | A1 | 19850816 | ES 1984-532997  | 19840531 |
|            |    |          | WO 1982-JP437   | 19821110 |
| SU 1322983 | A3 | 19870707 | SU 1984-3827995 | 19841224 |
|            |    |          | WO 1982-JP437   | 19821110 |

IT 92602-27-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

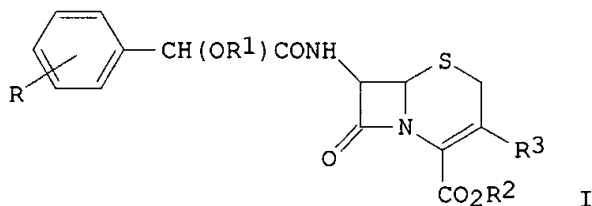
RN 92602-27-2 CAPLUS

CN L-Phenylalanine, 2-[[[2-[[1-(acetyloxy)ethoxy]carbonyl]-3-[[5-methyl-1,3,4-thiadiazol-2-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl]amino]-2-oxo-1-phenylethyl ester, monohydrochloride, [6R-[6.alpha.,7.beta.(R\*)]]- (9CI) (CA INDEX NAME)



● HCl

GI

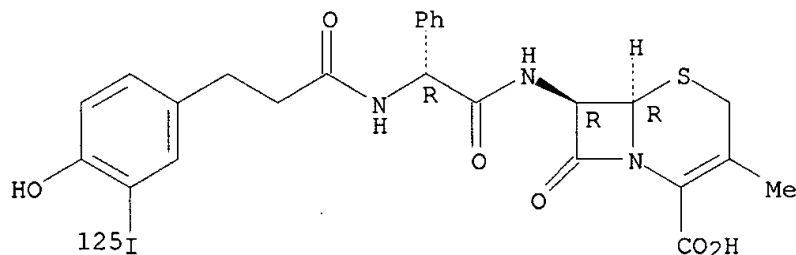


AB Cephalosporins I (R = H, OH; R1 = amino acid residue; R2 = 1-alkanoyloxyalkyl, 1-alkoxycarbonyloxyalkyl, phthalidyl, 5-methyl-2-oxo-1,3-dioxolan-4-ylmethyl; R3 = carbamoyloxymethyl, heterocyclylthiomethyl) were prepd. Thus D-HOCHPhCO2CHPh2 was treated with Me3CO2CNHCH2CO2H to give D-Me3CO2CNHCH2CO2CHPhCO2CHPh2 which was hydrogenolyzed and used to acylate the 7-aminocephem, followed by deblocking, to give I (R = H, R1 = H2NCH2CO, R2 = CH2O2CCMe3, R3 = 1-methyl-5-tetrazolylthiomethyl, II). At a dose corresponding to 125 mg of the free acid II was 38.0% excreted in the urine in 8 h.

L4 ANSWER 118 OF 148 CAPLUS COPYRIGHT 2003 ACS

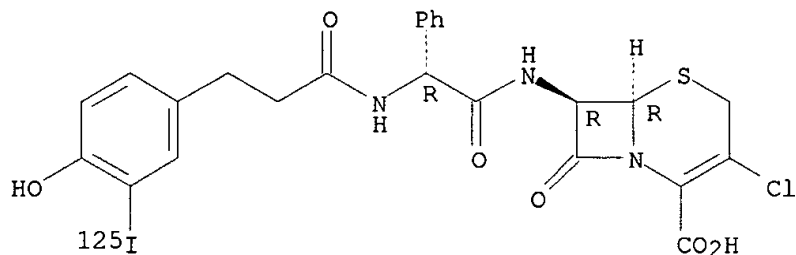
AN 1984:451568 CAPLUS  
 DN 101:51568  
 TI Binding of 125I-labeled .beta.-lactam antibiotics to the penicillin binding proteins of Escherichia coli  
 AU Rojo, Fernando; Ayala, Juan A.; De la Rosa, Enrique J.; De Pedro, Miguel A.; Aran, Vicente; Berenguer, Jose; Vazquez, David  
 CS Fac. Cien., Univ. Auton. Madrid, Madrid, Spain  
 SO Journal of Antibiotics (1984), 37(4), 389-93  
 CODEN: JANTAJ; ISSN: 0021-8820  
 DT Journal  
 LA English  
 IT **90986-75-7 90986-77-9**  
 RL: PROC (Process)  
 (penicillin-binding proteins preferential binding of)  
 RN 90986-75-7 CAPLUS  
 CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[[3-[4-hydroxy-3-(iodo-125I)phenyl]-1-oxopropyl]amino]phenylacetyl]amino]-3-methyl-8-oxo-, [6R-[6.alpha.,7.beta.(R\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 90986-77-9 CAPLUS  
 CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-chloro-7-[[[3-[4-hydroxy-3-(iodo-125I)phenyl]-1-oxopropyl]amino]phenylacetyl]amino]-8-oxo-, [6R-[6.alpha.,7.beta.(R\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB 125I-labeled derivs. of the .beta.-lactam antibiotics cephalixin, cephradine, cefaclor, and 6-.alpha.-aminopenicillanic acid were obtained by reacting these compds. with (125I)-Bolton-Hunter reagent. Target proteins were found in E. coli. The derivs. of cephalixin, cefaclor, and cephradine preferentially interact with the high-mol.-wt. penicillin binding proteins (PBP1a and PBP1b). The 125I-deriv. of

6-.alpha.-aminopenicillanic acid was preferentially bound by the low-mol.-wt. penicillin binding proteins 4 and 5/6. The iodinated derivs. showed a very high affinity of binding to their target proteins with apparent half-satg. concns. in the nM range.

L4 ANSWER 119 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1984:47629 CAPLUS

DN 100:47629

TI Binding specificities of penicillin-binding proteins - a conformational approach

AU Rao, V. S. R.

CS Mol. Biophys. Unit, Indian Inst. Sci., Bangalore, 560 012, India

SO Target Penicillin: Murein Sacculus Bact. Cell Walls Archit. Growth, Proc., Int. FEMS Symp. (1983), 359-67. Editor(s): Hakenbeck, Regine; Hoeltje, Joachim-Volker; Labischinski, Harald. Publisher: de Gruyter, Berlin, Fed. Rep. Ger.

CODEN: 50ODAA

DT Conference

LA English

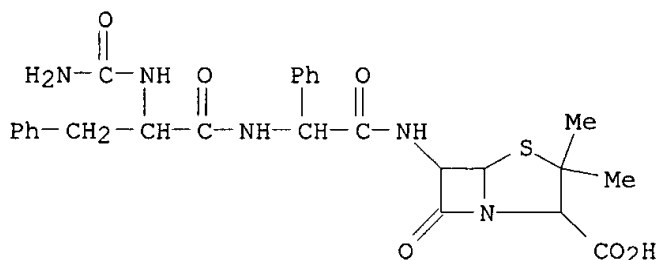
IT 54984-13-3 68964-66-9 68964-69-2  
68985-99-9

RL: PRP (Properties)

(conformation of, .beta.-lactamase and transpeptidase binding in relation to)

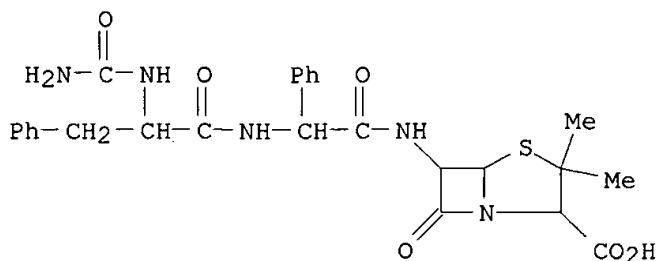
RN 54984-13-3 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-L-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



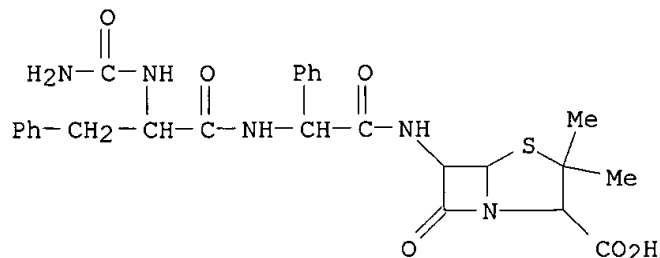
RN 68964-66-9 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



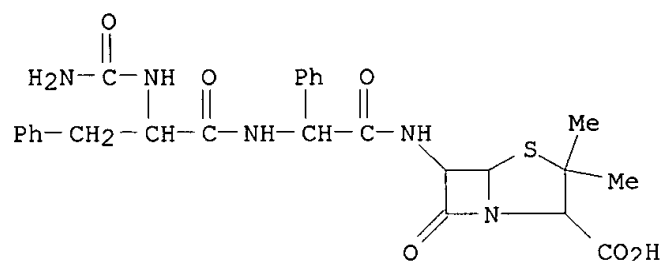
RN 68964-69-2 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-L-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-L-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



RN 68985-99-9 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-L-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



AB Ab initio MO calcns. of the .beta.-lactam antibiotics (cephams, phenams, thienamycins, penicillins) indicate that the nonplanarity of the N atom and conjugation by inclusion of a double bond leads to weakening of the peptide bond, the bond susceptible to .beta.-lactamase hydrolysis. Thus, the peptide bond in penicillins is weakened mainly due to the pyramidal character of N and in cephams (cephalosporins) due to resonance with the double bond; in highly active thienamycins, the peptide bond is weakened by both mechanisms. The overall shape of the antibiotic is also of importance in achieving a proper conformational fit in the .beta.-lactamase or transpeptidase active site. The compact conformation favored by penicillin G1, D-ampicillin, and 3-pyridylmethylpenicillin may be assocd. with, or initiate, the binding process in interactions with transpeptidase of gram-pos. bacteria. Substitutions at the 6.beta. side group of penicillanic acid, which favor extended conformation, result in good antibacterial properties against gram-pos. bacteria; the chiral center at C-27 does not affect those properties. However, changes in conformation beyond C-17 do affect the antibacterial activity against gram-neg. bacteria, suggesting that their transpeptidases are more specific than those of gram-pos. bacteria.

L4 ANSWER 120 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1983:505050 CAPLUS

DN 99:105050



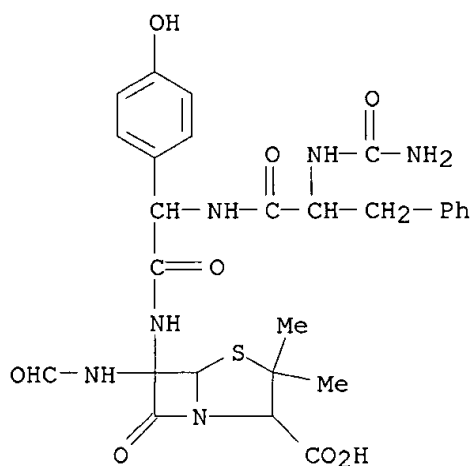
TI .beta.-Lactam antibacterial agents  
 IN Milner, Peter Henry  
 PA Beecham Group PLC, UK  
 SO Eur. Pat. Appl., 282 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 1

|    | PATENT NO.                                    | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 71395                                      | A1   | 19830209 | EP 1982-303821  | 19820721 |
|    | EP 71395                                      | B1   | 19880810 |                 |          |
|    | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE |      |          |                 |          |
|    |   |      |          | GB 1981-23033   | 19810725 |
|    |   |      |          | GB 1981-23034   | 19810725 |
|    |   |      |          | GB 1981-36823   | 19811207 |
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|    |   |      |          | GB 1982-7966    | 19820318 |
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|    |   |      |          | GB 1982-9954    | 19820403 |
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|    |   |      |          | GB 1982-21059   | 19820721 |
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|    | GB 2107307                                    | B2   | 19860226 |                 |          |
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|    |   |      |          | GB 1982-7966    | 19820318 |
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|    |   |      |          | GB 1982-15007   | 19820522 |
|    |   |      |          | EP 1982-303821  | 19820721 |
|    | NO 8202538                                    | A    | 19830126 | NO 1982-2538    | 19820723 |
|    | NO 162192                                     | B    | 19890814 |                 |          |
|    | NO 162192                                     | C    | 19891122 |                 |          |
|    |   |      |          | GB 1981-23033   | 19810725 |
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|    |   |      |          | GB 1982-15007   | 19820522 |
|    | FI 8202606                                    | A    | 19830126 | FI 1982-2606    | 19820723 |
|    | FI 78702                                      | B    | 19890531 |                 |          |
|    | FI 78702                                      | C    | 19890911 |                 |          |
|    |   |      |          | GB 1981-23033   | 19810725 |
|    |   |      |          | GB 1981-23034   | 19810725 |

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|            |    |          | GB 1981-36823  | 19811207 |
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| ES 514308  | A1 | 19831201 | ES 1982-514308 | 19820723 |
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| AU 568062  | B2 | 19871217 |                |          |
|            |    |          | GB 1981-23033  | 19810725 |
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|            |    |          | GB 1982-15007  | 19820522 |
| US 4539149 | A  | 19850903 | US 1982-401266 | 19820723 |
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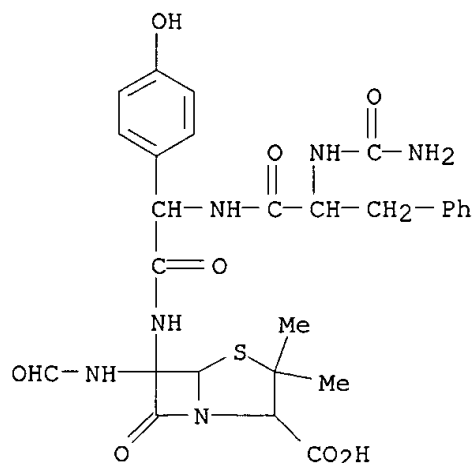
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| PL 145252   | B1 | 19880831 | GB 1982-15007  | 19820522 |
|             |    |          | PL 1982-237640 | 19820723 |
|             |    |          | GB 1981-23033  | 19810725 |
|             |    |          | GB 1981-23034  | 19810725 |
|             |    |          | GB 1981-36823  | 19811207 |
|             |    |          | GB 1981-36824  | 19811207 |
|             |    |          | GB 1982-7966   | 19820318 |
|             |    |          | GB 1982-9953   | 19820403 |
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| PL 146092   | B1 | 19881231 | GB 1982-15007  | 19820522 |
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| JP 58038288 | A2 | 19830305 | GB 1982-15007  | 19820522 |
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| IL 67222    | A1 | 19860429 | GB 1982-15007  | 19820522 |
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| ES 520953   | A1 | 19840516 | GB 1982-15007  | 19820522 |
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|             |    |          | GB 1981-23033  | 19810725 |
| US 4609652  | A  | 19860902 | GB 1981-23034  | 19810725 |
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|             |    |          | US 1985-694622 | 19850124 |
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|    |  |  | GB 1981-36823  | 19811207 |
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|    |  |  | GB 1985-14519  | 19850607 |
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| OS | CASREACT 99:105050   |  |                |          |
| IT | <b>86061-97-4P</b>   |  |                |          |
|    | RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  |  |                |          |
|    | (prepn. and bactericidal activity of)  |  |                |          |
| RN | 86061-97-4 CAPLUS  |  |                |          |
| CN | Glycinamide, N-(aminocarbonyl)-D-phenylalanyl-N-[2-carboxy-6-(formylamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-D-2-(4-hydroxyphenyl)-, monosodium salt, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI)<br>(CA INDEX NAME) |  |                |          |

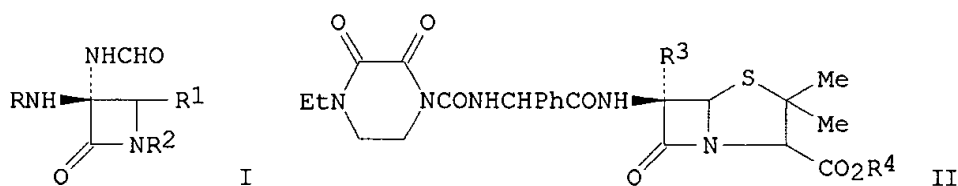


● Na

|    |  |  |  |  |
|----|--|--|--|--|
| IT | <b>86117-42-2P</b>   |  |  |  |
|    | RL: SPN (Synthetic preparation); PREP (Preparation)  |  |  |  |
|    | (prepn. of)  |  |  |  |
| RN | 86117-42-2 CAPLUS  |  |  |  |
| CN | Glycinamide, N-(aminocarbonyl)-D-phenylalanyl-N-[2-carboxy-6-(formylamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-D-2-(4-hydroxyphenyl)-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME) |  |  |  |



GI



AB .beta.-Lactams I (R = H, acyl; R1R2 = atoms required to complete a penam, cephem, or oxadithiacephem system) were prepd. Thus II (R3 = SMe, R4 = CH2Ph) was treated with NH3 to give II (R3 = NH2, R4 = CH2Ph) which was formylated with HCO2Ac to give II (R3 = NHCHO, R4 = CH2Ph). Hydrogenolysis of the ester group and treatment with BuCHEtCO2Na gave II (R3 = NHCHO, R4 = Na) which had a min. inhibitory concn. against *Proteus mirabilis* 889 of 0.2 .mu.g/mL.

L4 ANSWER 121 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1983:499494 CAPLUS

DN 99:99494

TI A study of the applicability of QSAR calculations for peptide hormones

AU Nadasdi, L.; Medzihradszky, K.

CS Peptidkem. Tansz. Kutato Csoport, Magy. Tud. Akad., Budapest, Hung.

SO Kemiai Kozlomenyek (1982), 58(4), 410-15

CODEN: KEKOAS; ISSN: 0022-9814

DT Journal

LA Hungarian

IT 57356-92-0

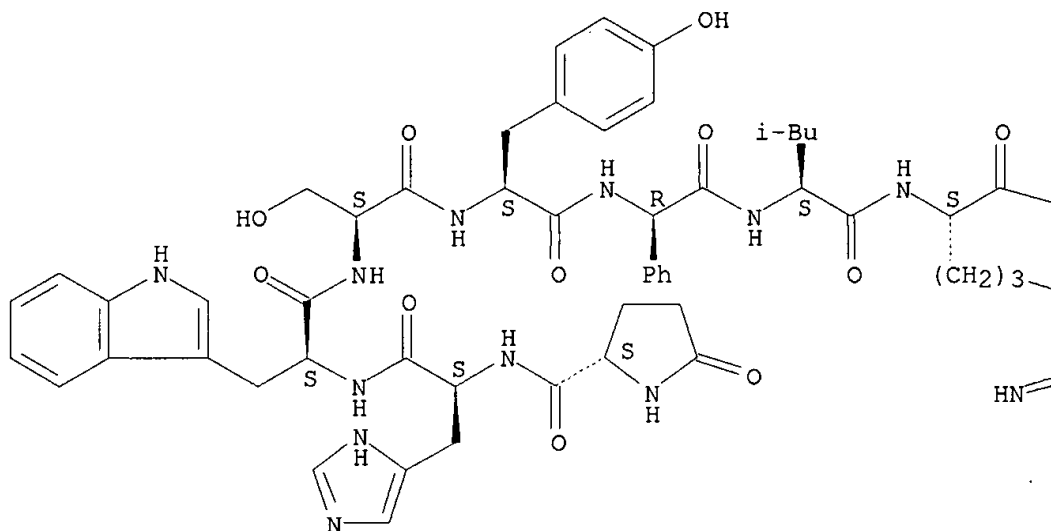
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (biol. activity of, structure in relation to)

RN 57356-92-0 CAPLUS

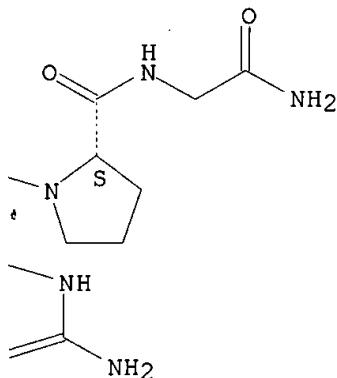
CN Luteinizing hormone-releasing factor (swine), 6-(D-2-phenylglycine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



AB Quant. structure-activity relations were calcd. for LH-RH analogs substituted in position 6 with D-Ala, D-Leu, D-Glu, D-Phe, D-Trp, and other D-amino acids, and compared with data from the literature (Coy, D. H., et al., 1979). A very high correlation and statistically-significant equations at a 95% confidence limit were obtained using lipophilic .pi. and steric .gamma. parameters. The lipophilic parameters are the most important with resp. to biol. activity.

L4 ANSWER 122 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1983:59889 CAPLUS  
 DN 98:59889

TI Improving intestinal absorption of cephalosporin derivatives  
 IN Nishikido, Joji; Kodama, Eiji; Shibukawa, Mitsuru  
 PA Asahi Chemical Industry Co., Ltd., Japan  
 SO Eur. Pat. Appl., 63 pp.  
 CODEN: EPXXDW

DT Patent  
 LA English

FAN.CNT 1

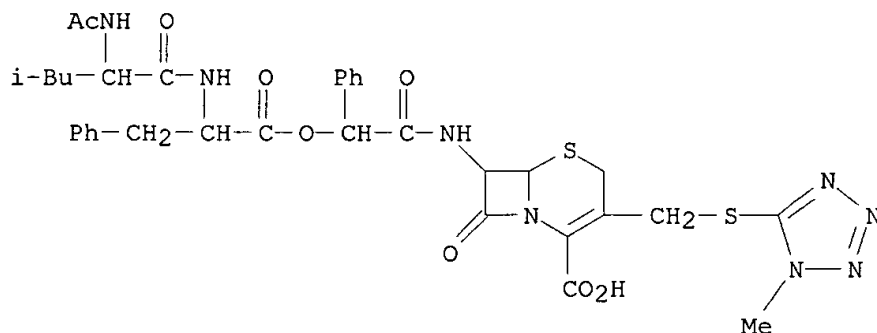
|    | PATENT NO.                                | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 60422                                  | A2   | 19820922 | EP 1982-101508  | 19820226 |
|    | EP 60422                                  | A3   | 19830824 |                 |          |
|    | R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE |      |          |                 |          |
|    |   |      |          | JP 1981-26743   | 19810227 |
|    |   |      |          | JP 1981-128688  | 19810819 |
|    | JP 57142988                               | A2   | 19820903 | JP 1981-26743   | 19810227 |
|    | JP 58032885                               | A2   | 19830225 | JP 1981-128688  | 19810819 |
|    | US 4465668                                | A    | 19840814 | US 1982-351613  | 19820224 |
|    |   |      |          | JP 1981-26743   | 19810227 |
|    |   |      |          | JP 1981-128688  | 19810819 |

IT 84294-10-0 84330-79-0

RL: PROC (Process)  
 (absorption of, by intestine)

RN 84294-10-0 CAPLUS

CN L-Phenylalanine, N-(N-acetyl-L-leucyl)-, 2-[[2-carboxy-3-[[[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl]amino]-2-oxo-1-phenylethyl ester, [6R-[6.alpha.,7.beta.(R\*)]]- (9CI)  
 (CA INDEX NAME)



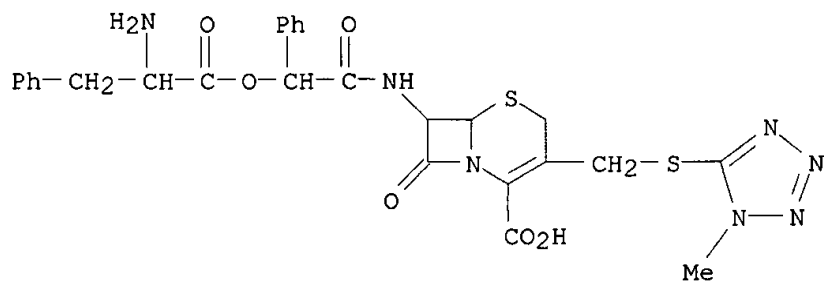
RN 84330-79-0 CAPLUS

CN L-Phenylalanine, 2-[[2-carboxy-3-[[[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl]amino]-2-oxo-1-phenylethyl ester, [6R-[6.alpha.,7.beta.(R\*)]]-, monoformate (9CI) (CA INDEX NAME)

CM 1

CRN 84330-78-9

CMF C27 H27 N7 O6 S2



CM 2

CRN 64-18-6

CMF C H2 O2

O=CH-OH

IT 84330-75-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and intestinal absorption of)

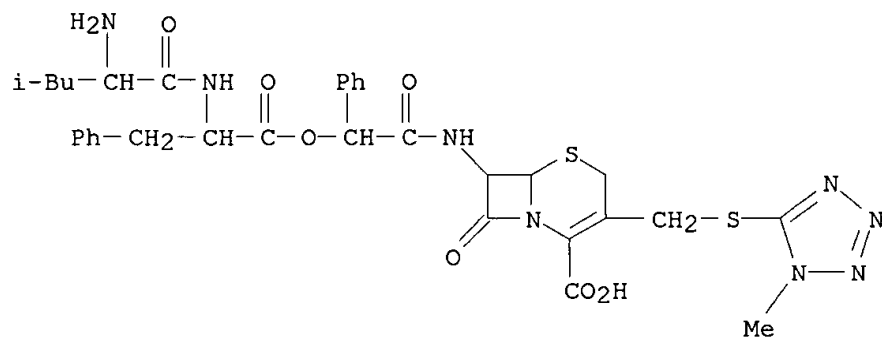
RN 84330-75-6 CAPLUS

CN L-Phenylalanine, N-L-leucyl-, 2-[[2-carboxy-3-[[[1-methyl-1H-tetrazol-5-yl]thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl]amino]-2-oxo-1-phenylethyl ester, [6R-[6.alpha.,7.beta.(R\*)]]-, monoformate (9CI) (CA INDEX NAME)

CM 1

CRN 84330-74-5

CMF C33 H38 N8 O7 S2



CM 2

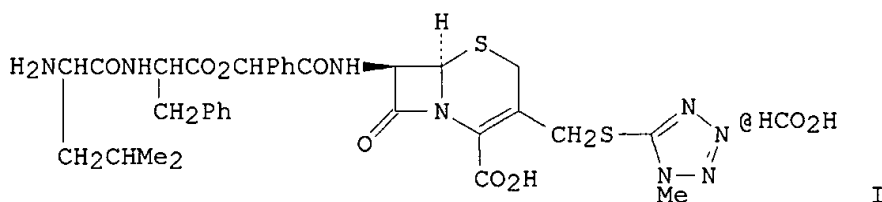
CRN 64-18-6

CMF C H2 O2



O=CH-OH

GI



AB Intestinal absorption of cephalosporins with low oral activity is improved by binding to any side chain in the 3-, 4-, or 7-position of a 7-aminocephalosporanic acid deriv., an oligopeptide X(NHCHR1CO)nNHCHR2CO (X = H, C1-15 alkyl or R3CO; R1 and R2 = side chain of an amino acid constituting the oligopeptide; R3 = H or C1-15 alkyl or protective group easily removable by acid hydrolysis, hydrogenolysis, or enzyme existing in a living body; n = 1-3). Thus, 7-[D-(O-L-leucyl-L-phenylalanyl)mandelamido]-3-[[1-methyl-1H-tetrazol-5-yl]thio]methyl]-3-cephem-4-carboxylic acid monoformate (I) [84330-75-6] was prepd. and administered to male rats at 50 mg/kg. The blood concn. was 4.51 .mu.g/mL 30 min after administration, as compared with 0.29 .mu.g/mL for the cephemcarboxylic acid deriv. without the oligopeptide.

L4 ANSWER 123 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1982:174580 CAPLUS

DN 96:174580

TI Evolution of design and achievement of inhibitors of the luteinizing hormone-releasing hormone as inhibitors of ovulation

AU Folkers, Karl; Humphries, John; Bowers, Cyril Y.

CS Inst. Biomed. Res., Univ. Texas, Austin, TX, 78712, USA

SO Zeitschrift fuer Naturforschung, Teil B: Anorganische Chemie, Organische Chemie (1982), 37B(2), 246-59  
CODEN: ZNBAD2; ISSN: 0340-5087

DT Journal

LA English

IT 81419-11-6

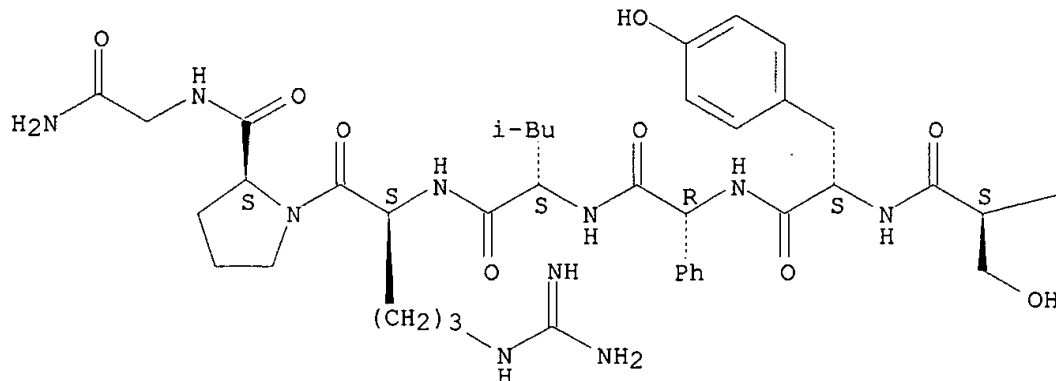
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ovulation-inhibiting activity of, structure in relation to)

RN 81419-11-6 CAPLUS

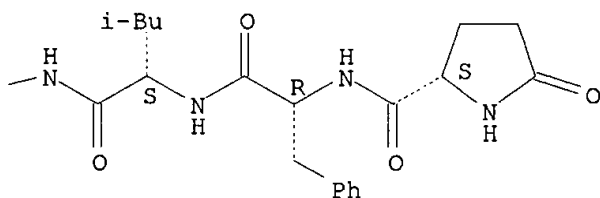
CN Luteinizing hormone-releasing factor (swine), 2-D-phenylalanine-3-L-leucine-6-(D-2-phenylglycine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



AB Structure-activity relations of LH-RH [9034-40-6] analogs as inhibitors of LH [9002-67-9] release and ovulation in rats and rhesus monkeys were studied. Inhibitory activities for >100 peptides are given. However, some analogs, e.g. [D-Phe<sub>2</sub>,Ala<sub>4</sub>,D-Phe<sub>6</sub>]-LH-RH [81419-23-0] (100 .mu.g) released LH and FSH [9002-68-0] at a ratio of LH/FSH greater than that induced by LH-RH. [D-Phe<sub>2</sub>,Pro<sub>3</sub>,D-Phe<sub>6</sub>]-LH-RH [64789-67-9] (6 S.c. injections of 50 mg every 8 h) inhibited ovulation and the action of endogenous LH-RH in cycling rhesus monkeys. Infusion of [D-Phe<sub>2</sub>,Pro<sub>3</sub>,D-Trp<sub>6</sub>]-LH-RH [60961-52-6] (375 .mu.g/day for 4 days) from a s.c. implanted minipump inhibited ovulation in cycling female rats and inhibited LH release in castrated male rats. Infusion of LH-RH (375 .mu.g/day, 4 days) and [D-Ala<sub>6</sub>,de-Gly<sub>10</sub>]-LH-RH EtNH<sub>2</sub> [52435-06-0] (6 .mu.g/day, 4 days) blocked uterine implantation sites of mated rats. Antagonist analogs with 3-proline and 3-leucine residues did not block the implantation sites indicating a difference in mechanism of contraception for agonists and antagonists of LH-RH. Solid phase synthesis of the peptides is also discussed.

L4 ANSWER 124 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1981:462724 CAPLUS  
 DN 95:62724  
 TI Antioviulatory decapeptides  
 IN Sarantakis, Dimitrios

PA American Home Products Corp., USA

SO U.S., 4 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
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|    |            |      |          | US 1979-104599  | 19791217 |

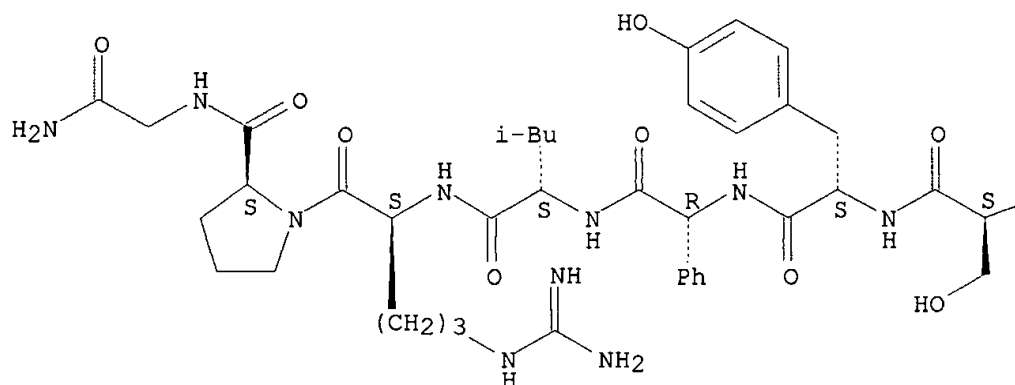
IT **78255-76-2P**RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 78255-76-2 CAPLUS

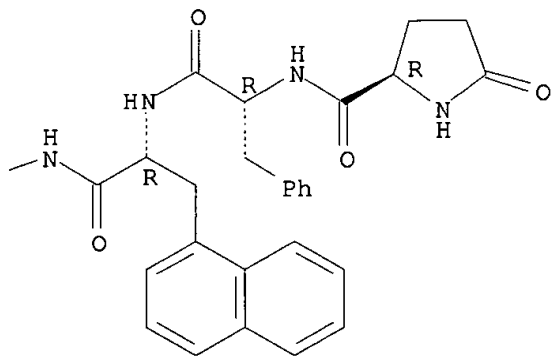
CN Luteinizing hormone-releasing factor (swine), 1-(5-oxo-D-proline)-2-D-phenylalanine-3-[3-(1-naphthalenyl)-D-alanine]-6-(D-2-phenylglycine)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



AB LH-releasing hormone antagonists D-pyroGlu-D-Phe-D-Nal-Ser-Tyr-X-Leu-Arg-Pro-Gly-NH<sub>2</sub> [I; D-Nal = 3-(1-naphthyl)-D-alanine residue; X = D-Nal, D-Trp, D-Phe, D-Tyr, D-Lys, D-Met, D-Ala, D-NHCHPhCO] were prepd. as ovulation inhibitors. Thus, I (X = D-Nal) (II) was prepd. by the solid-phase method on a benzhydrylamine resin. II at 500 .mu.g (s.c.) inhibited ovulation in rats by 70%.

L4 ANSWER 125 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1981:443678 CAPLUS

DN 95:43678

TI Pharmacologically active peptides

IN Gesellchen, Paul D.; Smiley, David L.

PA Lilly, Eli, and Co., USA

SO U.S., 12 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.            | KIND | DATE     | APPLICATION NO. | DATE     |
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| PI | US 4251439            | A    | 19810217 | US 1979-104345  | 19791217 |
|    | EP 30846              | A2   | 19810624 | EP 1980-304474  | 19801211 |
|    | EP 30846              | A3   | 19811223 |                 |          |
|    | EP 30846              | B1   | 19840509 |                 |          |
|    | R: DE, GB, LU, NL, SE |      |          |                 |          |
|    |                       |      |          | US 1979-104345  | 19791217 |
|    | GB 2065134            | A    | 19810624 | GB 1980-39662   | 19801211 |
|    | GB 2065134            | B2   | 19830602 |                 |          |
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|    | CA 1140539            | A1   | 19830201 | CA 1980-366540  | 19801211 |
|    |                       |      |          | US 1979-104345  | 19791217 |
|    | IL 61701              | A1   | 19840531 | IL 1980-61701   | 19801212 |
|    |                       |      |          | US 1979-104345  | 19791217 |
|    | BE 886676             | A1   | 19810616 | BE 1980-10077   | 19801216 |
|    |                       |      |          | US 1979-104345  | 19791217 |
|    | FR 2471969            | A1   | 19810626 | FR 1980-26690   | 19801216 |
|    | FR 2471969            | B1   | 19821105 |                 |          |
|    |                       |      |          | US 1979-104345  | 19791217 |
|    | JP 56097258           | A2   | 19810805 | JP 1980-179640  | 19801216 |
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|    | HU 29354              | O    | 19840130 | HU 1980-3010    | 19801216 |
|    | HU 185230             | B    | 19841228 |                 |          |
|    |                       |      |          | US 1979-104345  | 19791217 |
|    | CH 646685             | A    | 19841214 | CH 1980-9272    | 19801216 |
|    |                       |      |          | US 1979-104345  | 19791217 |

IT **78255-91-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. and analgesic activity of)

RN 78255-91-1 CAPLUS

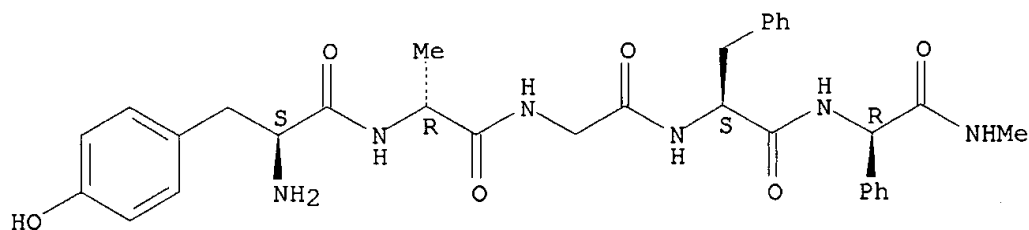
CN Glycinamide, L-tyrosyl-D-alanylglycyl-L-phenylalanyl-N-methyl-D-2-phenyl-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 78255-90-0

CMF C32 H38 N6 O6

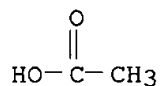
Absolute stereochemistry.



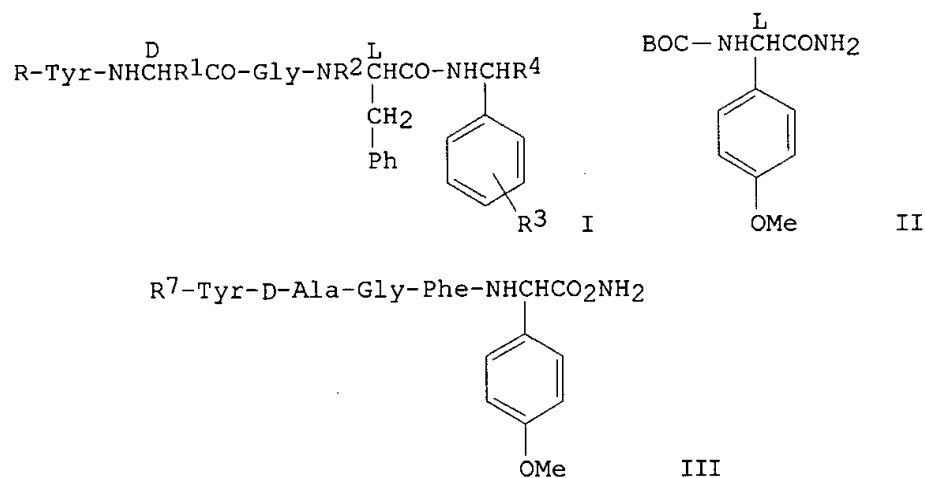
CM 2

CRN 64-19-7

CMF C2 H4 O2



GI



AB Enkephalin analogs I [ $R = H, C1-3$  alkyl;  $R1 = C1-4$  alkyl, allyl, cyclopropylmethyl,  $C1-2$  hydroxyalkyl,  $(CH_2)_mZMe$  ( $m = 1, 2$ ;  $Z = S, SO$ );  $R2 = H, C1-4$  alkyl, allyl, cyclopropylmethyl;  $R3 = H, halo, OH, C1-3$  alkoxy,  $NO_2, C1-3$  alkyl,  $CF_3$ ;  $R4 = CH_2OR_5$  ( $R_5 = H, C1-3$  alkyl),  $CONHR_5, CO_2R_6$  ( $R_6 = C1-3$  alkyl)] were prepd. as analgesics. Thus, phenylglycinamide II (BOC =  $Me_3CO_2C$ ) was BOC-deblocked and then coupled with BOC-Phe-OH by

DCC/1-hydroxybenzotriazole (HOBT) to give the protected dipeptide, which was BOC-deblocked and then coupled to BOC-Tyr-D-Ala-Gly-OH by DCC/HOBT to give peptide III (R7 = BOC). The latter was BOC-deblocked to give III (R7 = H). The analgesic activities of I were detd. in mice by the hot plate test.

L4 ANSWER 126 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1981:170508 CAPLUS

DN 94:170508

TI Penicillin-binding proteins of Escherichia coli identified with a 125I-derivative of ampicillin

AU Schwarz, U.; Seeger, K.; Wengenmayer, F.; Strecker, H.

CS Abt. Biochem., Max-Planck-Inst. Virusforsch., Tuebingen, Fed. Rep. Ger.

SO FEMS Microbiology Letters (1981), 10(2), 107-9

CODEN: FMLED7; ISSN: 0378-1097

DT Journal

LA English

IT 77471-26-2P

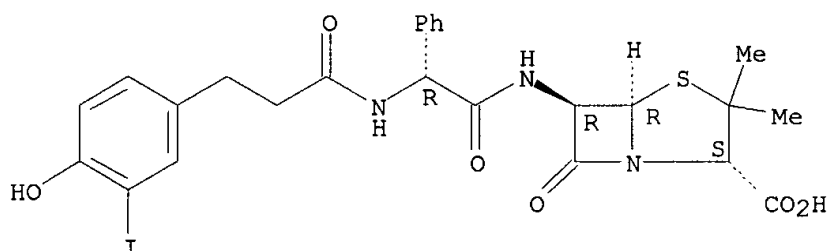
RL: PREP (Preparation)

(prepn. of and labeling by, of penicillin-binding proteins of Escherichia coli)

RN 77471-26-2 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[3-(4-hydroxy-3-iodophenyl)-1-oxopropyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB A 125I-labeled deriv. of ampicillin with high sp. activity was prepd. by using the Bolton-Hunter reagent, and the deriv. was used for the labeling of penicillin-binding proteins (PBPs) of E. coli membranes. The radiolabeled deriv. was purified by chromatog. on a Bio-Gel column before use in the binding assays. The binding pattern of 125I-labeled ampicillin, as detd. by autoradiog., was similar but not identical to that of penicillin G-14C. A new band was detected between PBP 1B and PBP 2. In competition studies with different .beta.-lactam antibiotics (mecillinam, cefotaxime, cefoxitin), the qual. and quant. competition in binding of 125I-labeled ampicillin was similar to that obtained with penicillin G-14C.

L4 ANSWER 127 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1981:168311 CAPLUS

DN 94:168311

TI A study of the applicability of QSAR calculation for peptide hormones

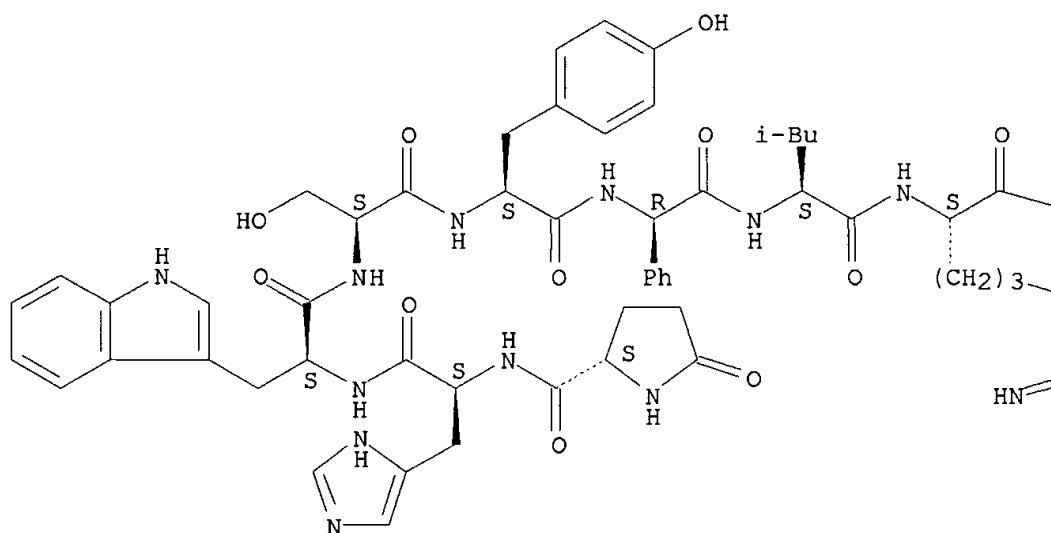
AU Nadasdi, Laszlo; Medzihradszky, Kalman

CS Inst. Org. Chem., Eotvos Lorand Univ., Budapest, 1088, Hung.

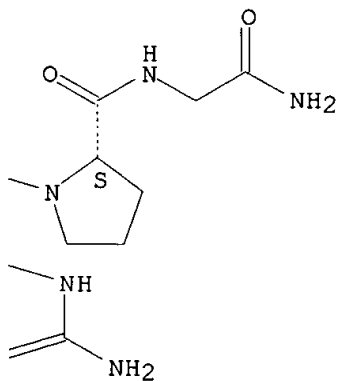
SO Biochemical and Biophysical Research Communications (1981), 99(2), 451-7  
CODEN: BBRCA9; ISSN: 0006-291X  
DT Journal  
LA English  
IT **57356-92-0**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(biol. activity of, structure in relation to)  
RN 57356-92-0 CAPLUS  
CN Luteinizing hormone-releasing factor (swine), 6-(D-2-phenylglycine)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



AB A quant. structure-activity relation (QSAR) was calcd. for the hypothalamic hormone LH-RH [33515-09-2]. A very good correlation and statistically significant equations at 95% confidence limit were obtained using information on the lipophilic nature and steric characteristics of the amino acid side chains.

L4 ANSWER 128 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1980:604632 CAPLUS

DN 93:204632

TI .beta.-Lactam compounds

IN Fujimoto, Yasuo

PA Nippon Chemiphar Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 4 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|-------------|------|----------|-----------------|----------|
| PI | JP 55040631 | A2   | 19800322 | JP 1978-113666  | 19780918 |
|    |             |      |          | JP 1978-113666  | 19780918 |

IT 75354-91-5P 75354-92-6P 75354-93-7P

75354-94-8P 75354-96-0P 75430-91-0P

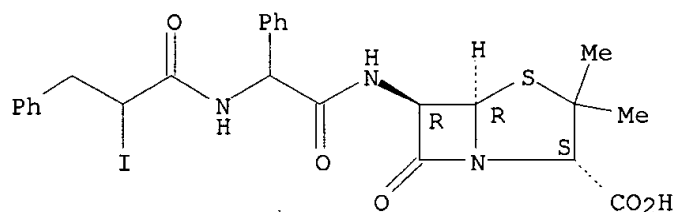
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. and bactericidal activity of)

RN 75354-91-5 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[(2-iodo-1-oxo-3-phenylpropyl)amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

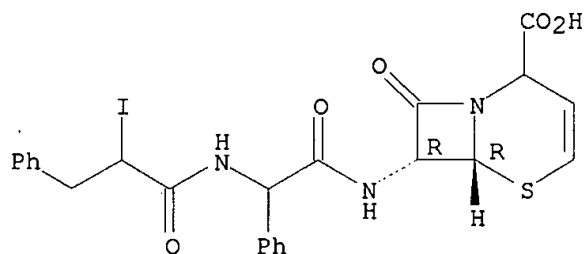


RN 75354-92-6 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-3-ene-2-carboxylic acid, 7-[[[(2-iodo-1-oxo-3-phenylpropyl)amino]phenylacetyl]amino]-8-oxo-, [6R-(6.alpha.,7.beta.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

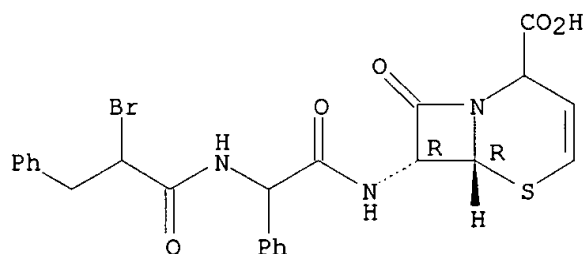




RN 75354-93-7 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-3-ene-2-carboxylic acid,  
7-[[[(2-bromo-1-oxo-3-phenylpropyl)amino]phenylacetyl]amino]-8-oxo-,  
[6R-(6.alpha.,7.beta.)]- (9CI) (CA INDEX NAME)

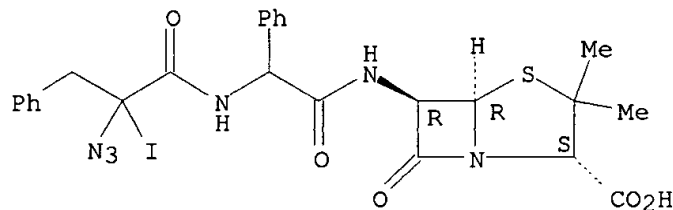
Absolute stereochemistry.



RN 75354-94-8 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[(2-azido-2-iodo-1-oxo-3-phenylpropyl)amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-,  
[2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

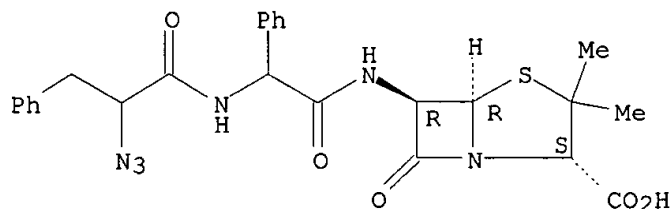
Absolute stereochemistry.



RN 75354-96-0 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[(2-azido-1-oxo-3-phenylpropyl)amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-,  
[2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

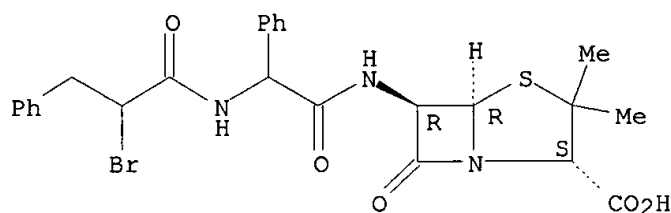
Absolute stereochemistry.



RN 75430-91-0 CAPLUS

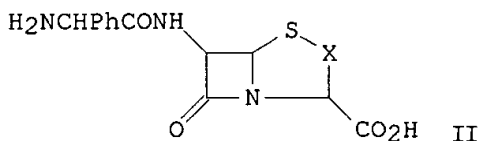
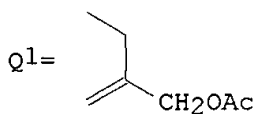
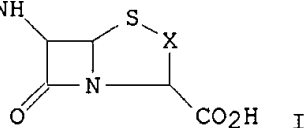
CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[(2-bromo-1-oxo-3-phenylpropyl)amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI

PhCRR<sup>2</sup>CR<sup>1</sup>R<sup>3</sup>CONHCHPhCONH



AB Seven .beta.-lactams D(-)-I (X = Q, Q1; R, R1 = H, a single bond; R2, R3 = H, halo, N3, or R2R3 form an aziridine ring) were prepd. by reaction of PhCRR<sup>2</sup>CR<sup>1</sup>R<sup>3</sup>CO<sub>2</sub>H with II. Min. inhibitory concns. of I were given against *S. aureus*, *E. coli*, *Kl. pneumoniae*, *P. vulgaris*, and *P. aeruginosa*. Thus, 102 g PhCH<sub>2</sub>CHICO<sub>2</sub>H was stirred with (COCl)<sub>2</sub> in THF 1 h with ice cooling, stripped of excess (COCl)<sub>2</sub>, a mixt. of 150 mg ampicillin and KHCO<sub>3</sub> in aq. THF added at pH 7.5-8.0, and the whole stirred 40 m with ice cooling to give D(-)-I 89.8% (X = Q, R = R2 = R3 = H, R1 = iodo).

L4 ANSWER 129 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1980:472308 CAPLUS  
 DN 93:72308  
 TI Analgesic polypeptide  
 IN Sarantakis, Dimitrios  
 PA American Home Products Corp., USA  
 SO U.S., 4 pp.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | US 4196122 | A    | 19800401 | US 1977-812039  | 19770701 |
|    |            |      |          | US 1977-812039  | 19770701 |

IT **74412-05-8P**

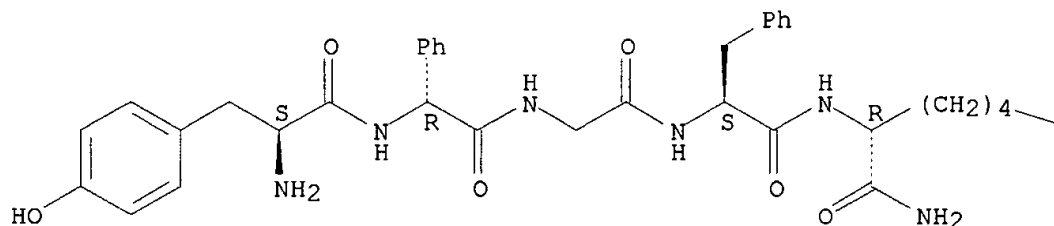
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (prepn. and analgesic activity of)

RN 74412-05-8 CAPLUS

CN D-Lysinamide, L-tyrosyl-D-2-phenylglycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

NH2

IT **74412-04-7DP**, resin-bound

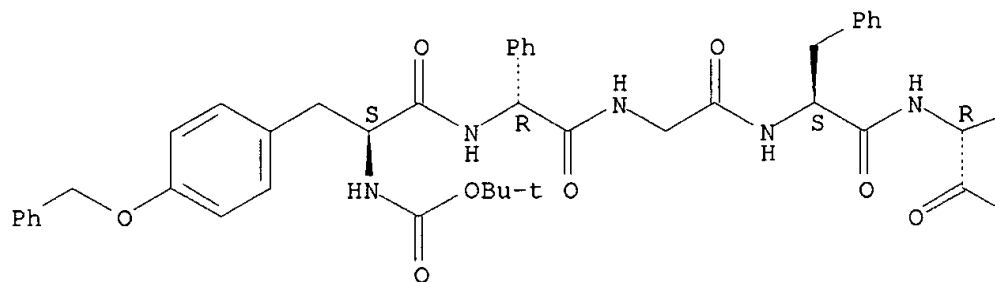
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and resin-cleavage and deblocking of)

RN 74412-04-7 CAPLUS

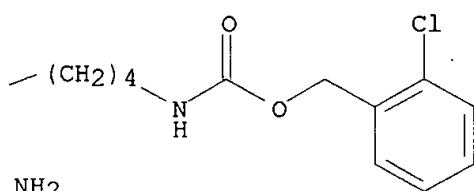
CN D-Lysinamide, N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-tyrosyl-D-2-phenylglycylglycyl-L-phenylalanyl-N6-[(2-chlorophenyl)methoxy]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



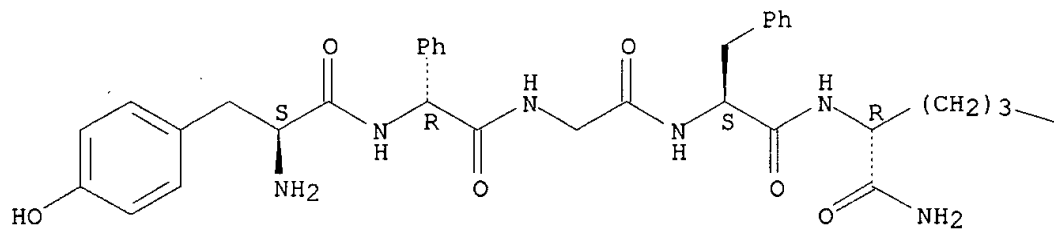
PAGE 1-B



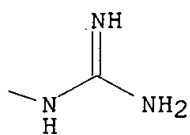
IT 74412-06-9P 74412-07-0P 74412-08-1P  
 74412-09-2P 74412-10-5P 74412-11-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 74412-06-9 CAPLUS  
 CN D-Argininamide, L-tyrosyl-D-2-phenylglycylglycyl-L-phenylalanyl- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



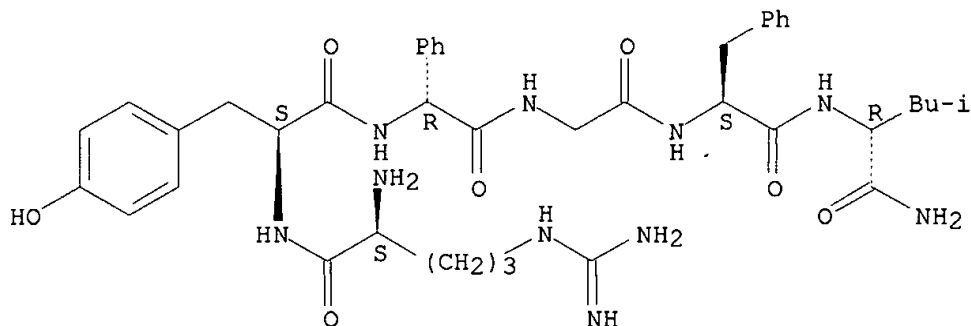
PAGE 1-B



RN 74412-07-0 CAPLUS

CN D-Leucinamide, L-arginyl-L-tyrosyl-D-2-phenylglycylglycyl-L-phenylalanyl-  
(9CI) (CA INDEX NAME)

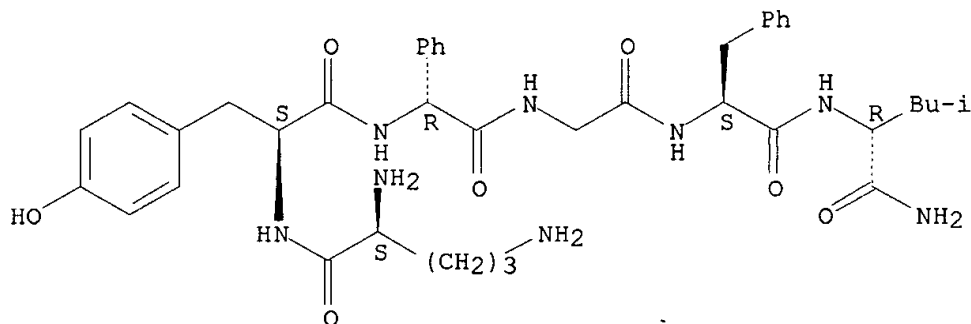
Absolute stereochemistry.



RN 74412-08-1 CAPLUS

CN D-Leucinamide, L-ornithyl-L-tyrosyl-D-2-phenylglycylglycyl-L-phenylalanyl-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

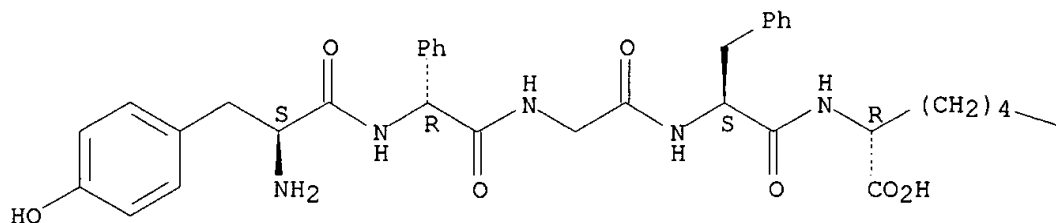


RN 74412-09-2 CAPLUS

CN D-Lysine, N2-[N-[N-(D-2-phenyl-N-L-tyrosylglycyl)glycyl]-L-phenylalanyl]-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

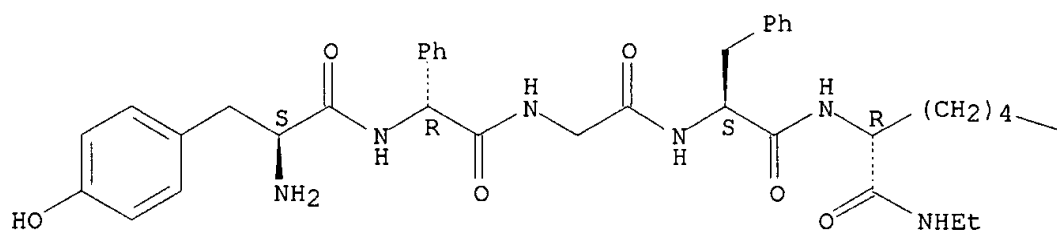
$$\text{—NH}_2$$

RN 74412-10-5 CAPLUS

CN D-Lysinamide, L-tyrosyl-D-2-phenylglycylglycyl-L-phenylalanyl-N-ethyl-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

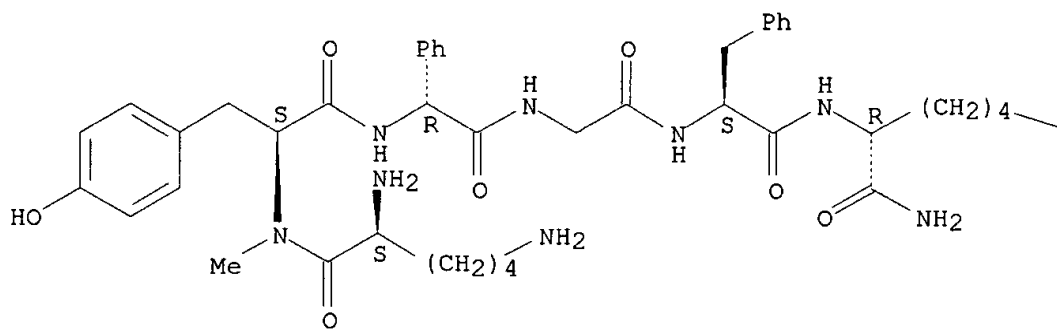
$$-\text{NH}_2$$

RN 74412-11-6 CAPLUS

CN D-Lysinamide, L-lysyl-N-methyl-L-tyrosyl-D-2-phenylglycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

—NH<sub>2</sub>

AB Enkephalin analogs H-X-X1-D-Phg-Gly-Phe-X3-R (Phg = HNCHPhCO; X = null, Arg, Lys, Orn; X1 = Tyr, MeTyr, N-allyl- or N-cyclopropylmethyltyrosine residue; X3 = D-Lys, D-Arg, D-Met, D-Leu; R = OH, NH<sub>2</sub>, NHCnH<sub>2n+1</sub> where n = 1-4) were prepd. as analgesics. Thus, BOC-D-Lys(ZCl-2)-OH (BOC = Me<sub>3</sub>CO<sub>2</sub>C, ZCl-2 = CO<sub>2</sub>CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>Cl-2) was amidated with benzhydrylamine resin (BHA-resin) to give BOC-D-Lys(ZCl-2)-NH-BHA-resin, which was extended by stepwise peptide couplings to BOC-Tyr(CH<sub>2</sub>Ph)-D-Phg-Gly-Phe-D-Lys(ZCl-2)-NH-BHA-resin. The latter was resin-cleaved and deblocked by HF/anisole to give H-Tyr-D-Phg-Gly-Phe-D-Lys-NH<sub>2</sub> (I). I at 1 mg/kg (i.v.) induced analgesic activity according to the rat-tail flick test.

L4 ANSWER 130 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1979:439466 CAPLUS

DN 91:39466

TI Penicillanic acid derivatives

IN Schwarz, Uli

PA Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Fed. Rep. Ger.

SO Ger. Offen., 12 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|-------------|------|----------|-----------------|----------|
| PI | DE 2739922  | A1   | 19790308 | DE 1977-2739922 | 19770905 |
|    | GB 2005254  | A    | 19790419 | GB 1978-35511   | 19780904 |
|    |             |      |          | DE 1977-2739922 | 19770905 |
|    | FR 2403344  | A1   | 19790413 | FR 1978-25546   | 19780905 |
|    |             |      |          | DE 1977-2739922 | 19770905 |
|    | JP 54048788 | A2   | 19790417 | JP 1978-109050  | 19780905 |
|    |             |      |          | DE 1977-2739922 | 19770905 |

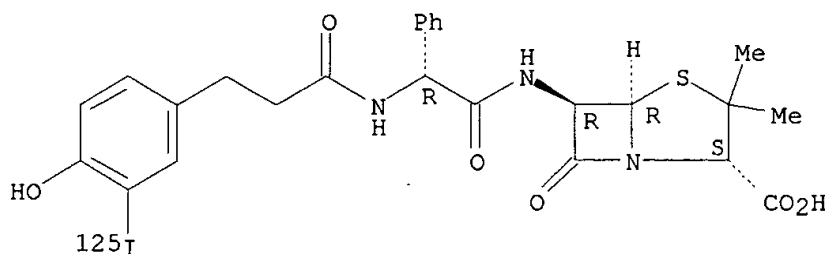
IT **70343-46-3P 70343-48-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 70343-46-3 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[3-[4-hydroxy-3-(iodo-125I)phenyl]-1-oxopropyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

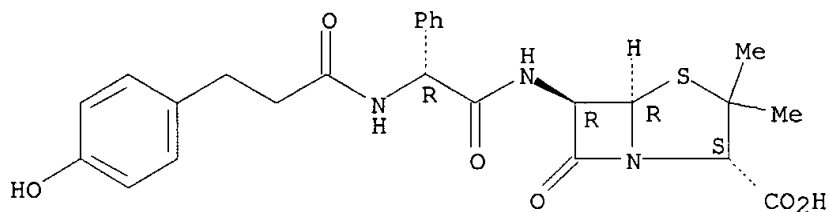
Absolute stereochemistry.



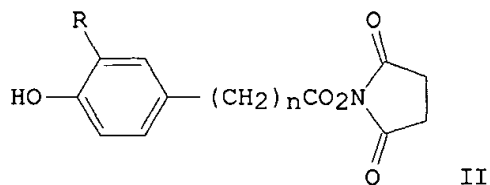
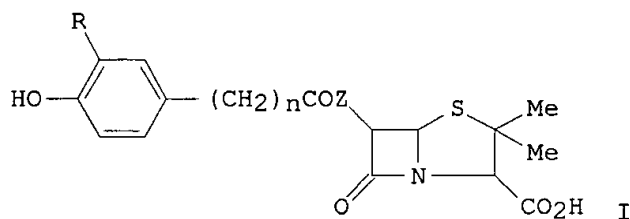
RN 70343-48-5 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[3-(4-hydroxyphenyl)-1-oxopropyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB Penicillanic acid derivs. I ( $n = 1-11$ ;  $R = \text{H, halo, OH, NO}_2, \text{Cl-4 alkyl or alkoxy}$ ;  $Z = \text{NH, NHCHPhCONH}$ ) were prepd. by the reaction of N-acyloxysuccinimides II with ampicillin or 6-aminopenicillanic acid. Thus, ampicillin reacted with II ( $R = 125\text{I}$ ,  $n = 2$ ) to give I ( $R = 125\text{I}$ ,  $n = 2$ ,  $Z = \text{NHCHPhCONH}$ ).

L4 ANSWER 131 OF 148 CAPLUS COPYRIGHT 2003 ACS



AN 1979:121187 CAPLUS  
 DN 90:121187  
 TI Aminoalcohol derivative  
 IN Lambelin, Georges; Roncucci, Romeo; Roba, Joseph; Gillet, Claude; Snyers, Michel  
 PA Continental Pharma, Belg.  
 SO Ger. Offen., 48 pp.  
 CODEN: GWXXBX  
 DT Patent  
 LA German  
 FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | DE 2817494 | A1   | 19781109 | DE 1978-2817494 | 19780421 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | GB 1603379 | A    | 19811125 | GB 1978-27732   | 19780427 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    |            |      |          | GB 1978-16813   | 19780427 |
|    | GB 1603378 | A    | 19811125 | GB 1978-16813   | 19780427 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | SE 7804897 | A    | 19781104 | SE 1978-4897    | 19780428 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | NL 7804621 | A    | 19781107 | NL 1978-4621    | 19780428 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | CA 1118438 | A1   | 19820216 | CA 1978-302239  | 19780428 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | US 4474977 | A    | 19841002 | US 1978-901223  | 19780428 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | IL 54608   | A1   | 19840131 | IL 1978-54608   | 19780501 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | FI 7801347 | A    | 19781104 | FI 1978-1347    | 19780502 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | DK 7801898 | A    | 19781104 | DK 1978-1898    | 19780502 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | NO 7801554 | A    | 19781106 | NO 1978-1554    | 19780502 |
|    | NO 146057  | B    | 19820413 |                 |          |
|    | NO 146057  | C    | 19820721 |                 |          |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | ZA 7802507 | A    | 19790725 | ZA 1978-2507    | 19780502 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    | ES 469843  | A1   | 19790916 | ES 1978-469843  | 19780502 |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |
|    | AT 7803179 | A    | 19800115 | AT 1978-3179    | 19780502 |
|    | AT 358020  | B    | 19800811 |                 |          |
|    |            |      |          | LU 1977-77236   | 19770503 |
|    |            |      |          | LU 1977-77237   | 19770503 |

|             |    |          |               |          |
|-------------|----|----------|---------------|----------|
| FR 2389597  | A1 | 19781201 | FR 1978-13202 | 19780503 |
| FR 2389597  | B1 | 19830819 |               |          |
|             |    |          | LU 1977-77236 | 19770503 |
|             |    |          | LU 1977-77237 | 19770503 |
| AU 7835733  | A1 | 19791108 | AU 1978-35733 | 19780503 |
| AU 517255   | B2 | 19810716 |               |          |
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|             |    |          | LU 1977-77237 | 19770503 |
| CH 635570   | A  | 19830415 | CH 1978-4836  | 19780503 |
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|             |    |          | LU 1977-77237 | 19770503 |
| JP 53141230 | A2 | 19781208 | JP 1978-53627 | 19780504 |
| JP 59040140 | B4 | 19840928 |               |          |
|             |    |          | LU 1977-77236 | 19770503 |
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| AT 7906288  | A  | 19810715 | AT 1979-6288  | 19790925 |
| AT 366023   | B  | 19820310 |               |          |
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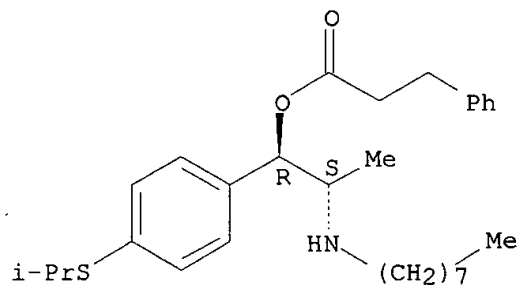
IT **69145-90-0**

RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. as muscle relaxant)

RN 69145-90-0 CAPLUS

CN Benzenepropanoic acid, 1-[4-[(1-methylethyl)thio]phenyl]-2-(octylamino)propyl ester, hydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

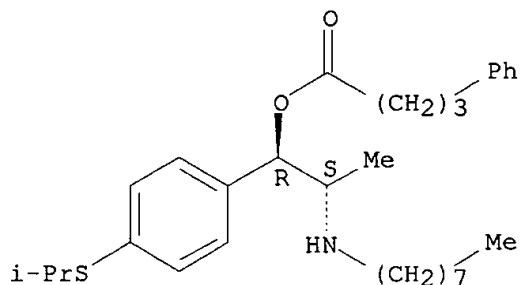
IT **69145-94-4P 69145-97-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 69145-94-4 CAPLUS

CN Benzenebutanoic acid, 1-[4-[(1-methylethyl)thio]phenyl]-2-(octylamino)propyl ester, hydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

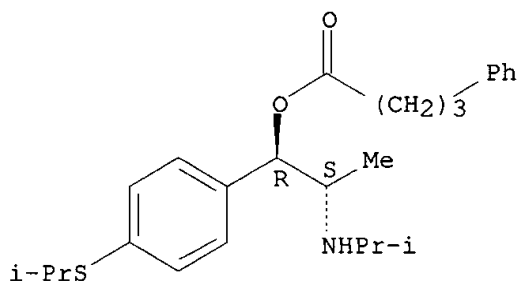


● HCl

RN 69145-97-7 CAPLUS

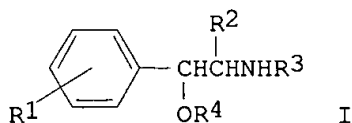
CN Benzenebutanoic acid, 2-[(1-methylethyl)amino]-1-[4-[(1-methylethyl)thio]phenyl]propyl ester, hydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

GI

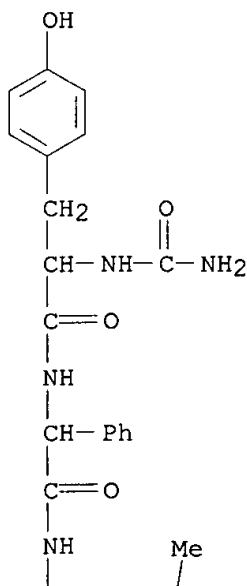


AB One hundred three amino alcs. I [R1 = H, C1-5 alkylthio, alkoxy, alkyl, C5-6 cycloalkylthio, cycloalkoxy, cycloalkyl, halo; R2 = C1-3 alkyl; R3 = C1-8 alkyl, C1-4 alkyl, optionally substituted with Ph, PhO, Bz, (un)substituted with alkyl, alkoxy, halo, C6-18 alkenyl, C5-9 cycloalkyl; R4 = COR5 [R5 = C1-10 alkyl, C2-4 alkenyl, C3-8 cycloalkyl, Ph (un)substituted with C1-3 alkyl, alkoxy, halo, C1-4 alkyl, (un)substituted with C1-3 carbalkoxy, alkoxy, NH2, acylamino, C5-6 cycloalkyl, PhO, Ph, optionally substituted with alkyl, alkoxy, halo, cinnamyl], H], useful as

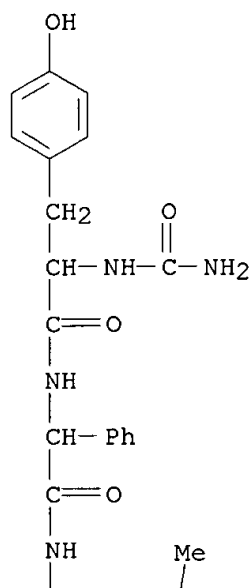
antihypertensives, peripheral vasodilators, muscle relaxants, platelet aggregation inhibitors, hypolipemics, and thrombosis inhibitors, were prepd. Thus, acylation of 4-Me2CHSC6H4CH(OH)CHMeNH(CH2)7Me by refluxing with AcCl in C6H6 or PrCOCl gave 70 or 52%, resp. of the corresponding 4-Me2CHSC6H4CH(OR4)CHMeNH(CH2)7Me (R4 = Ac, PrCO).

L4 ANSWER 132 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1979:49012 CAPLUS  
 DN 90:49012  
 TI .beta.-Lactam antibiotics. II. Structure-activity relationships of 6-[.alpha.-(.alpha.'-ureidoacylamino) acylamino] penicillanic acids  
 AU Ferres, Harry; Basker, Michael J.; Best, Desmond J.; Harrington, Frank P.; O'Hanlon, Peter J.  
 CS Chemother. Res. Cent., Beecham Pharm., Brockham Park/Betchworth/Surrey, UK  
 SO Journal of Antibiotics (1978), 31(10), 1013-22  
 CODEN: JANTAJ; ISSN: 0021-8820  
 DT Journal  
 LA English  
 IT 54896-24-1 54896-25-2 54896-27-4  
 54896-30-9 54896-31-0 54896-32-1  
 54896-34-3 54896-35-4 54896-46-7  
 54896-47-8 54896-49-0 54984-13-3  
 68929-98-6 68930-07-4 68964-66-9  
 68964-69-2 68964-77-2 68985-99-9  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (bactericidal activity of)  
 RN 54896-24-1 CAPLUS  
 CN Glycinamide, N-(aminocarbonyl)-D-tyrosyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

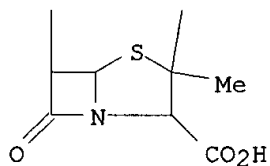
PAGE 1-A



PAGE 1-A



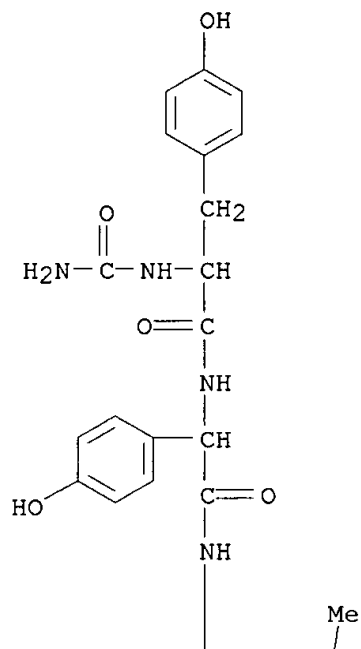
PAGE 2-A



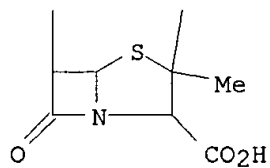
RN 54896-25-2 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-D-tyrosyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-(4-hydroxyphenyl)-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

PAGE 1-A

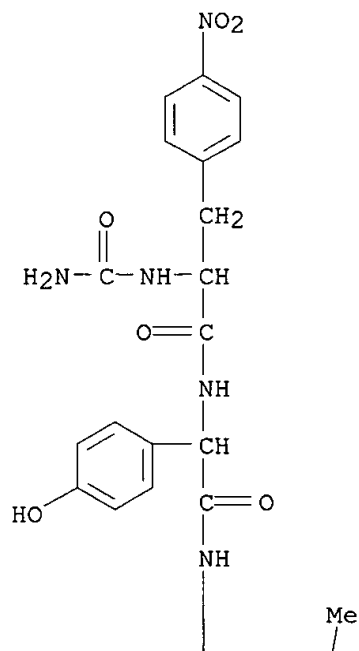


PAGE 2-A

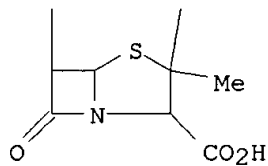


RN 54896-27-4 CAPLUS  
 CN Glycinamide, N-(aminocarbonyl)-4-nitrophenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-(4-hydroxyphenyl)-, (2R)-(9CI) (CA INDEX NAME)

PAGE 1-A



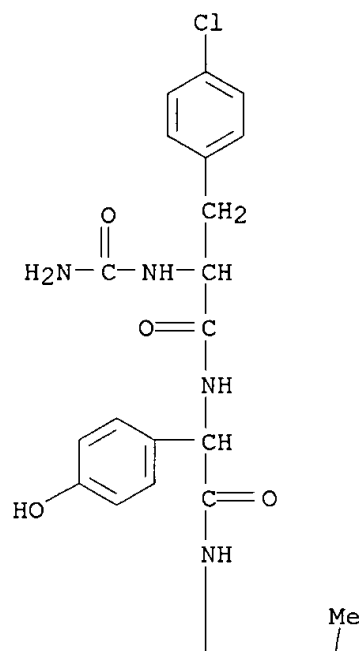
PAGE 2-A



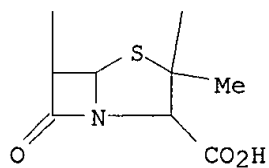
RN 54896-30-9 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-4-chlorophenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-(4-hydroxyphenyl)-, (2R)- (9CI) (CA INDEX NAME)

PAGE 1-A



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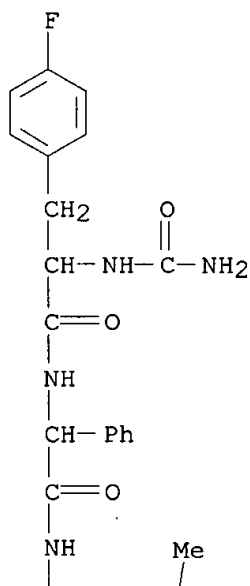


RN 54896-31-0 CAPLUS

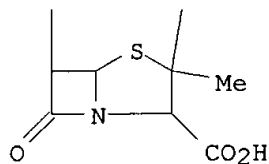
CN Glycinamide, N-(aminocarbonyl)-4-fluorophenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)-(9CI) (CA INDEX NAME)



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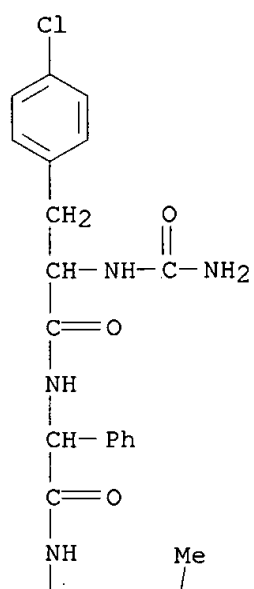


PAGE 2-A

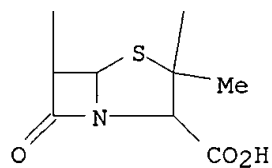


RN 54896-32-1 CAPLUS  
 CN Glycinamide, N-(aminocarbonyl)-4-chlorophenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)

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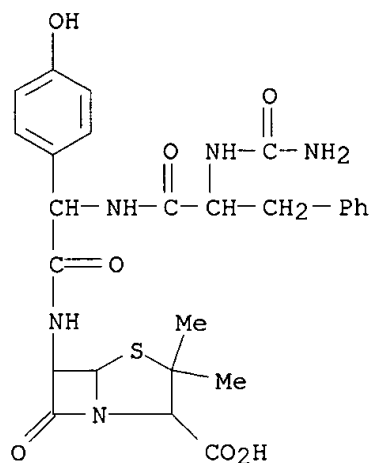


PAGE 2-A



RN 54896-34-3 CAPLUS

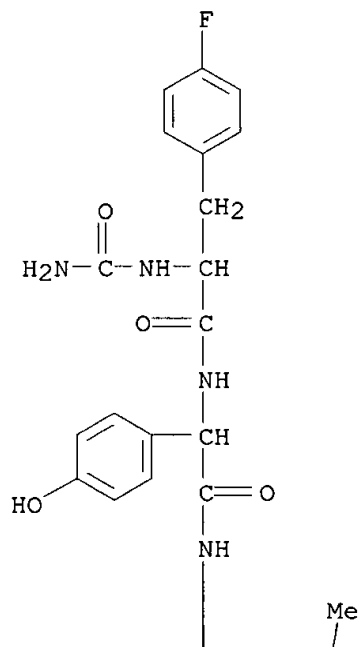
CN Glycinamide, N-(aminocarbonyl)-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-(4-hydroxyphenyl)-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



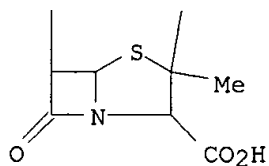
RN 54896-35-4 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-4-fluorophenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-(4-hydroxyphenyl)-, (2R)- (9CI) (CA INDEX NAME)

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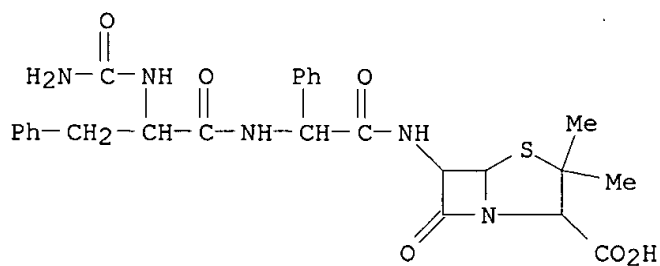


PAGE 2-A



RN 54896-46-7 CAPLUS

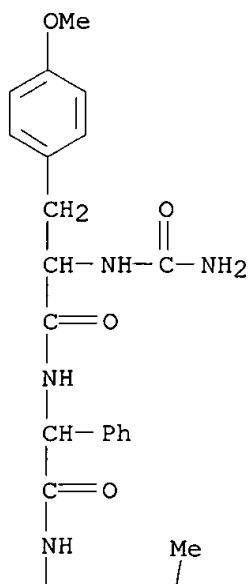
CN Glycinamide, N-(aminocarbonyl)phenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI)  
(CA INDEX NAME)



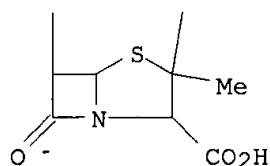
RN 54896-47-8 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-O-methyl-L-tyrosyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

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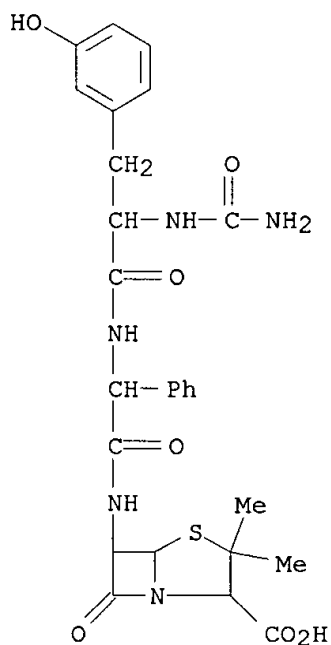


PAGE 2-A



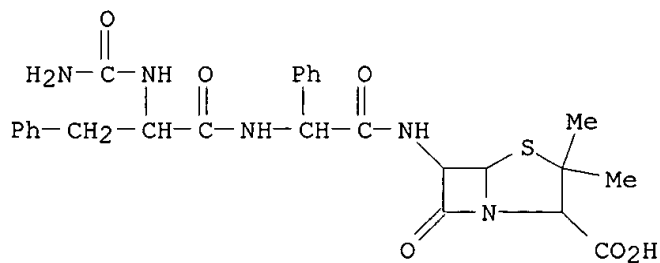
RN 54896-49-0 CAPLUS

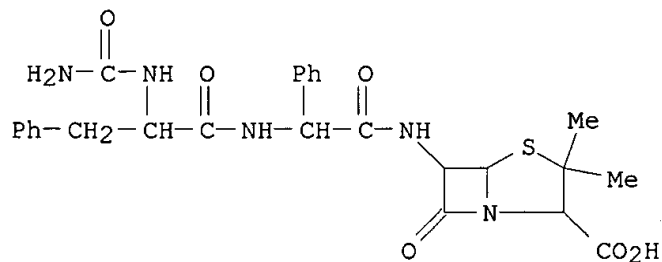
CN Glycinamide, N-(aminocarbonyl)-3-hydroxyphenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)



RN 54984-13-3 CAPLUS

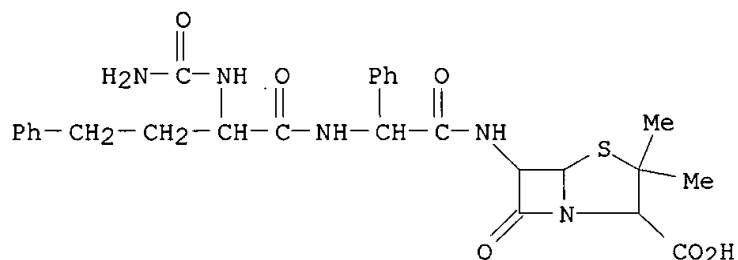
CN Glycinamide, N-(aminocarbonyl)-L-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)





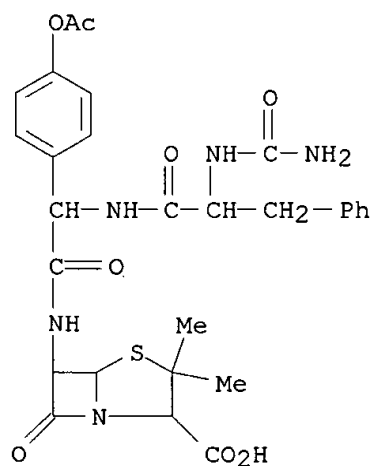
RN 68929-98-6 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[2-[(aminocarbonyl)amino]-1-oxo-4-phenylbutyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, stereoisomer (9CI) (CA INDEX NAME)



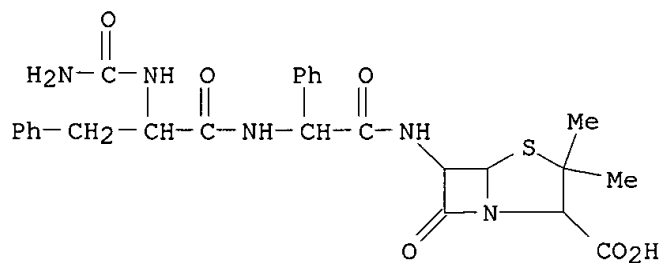
RN 68930-07-4 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-D-phenylalanyl-D-2-[4-(acetyloxy)phenyl]-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



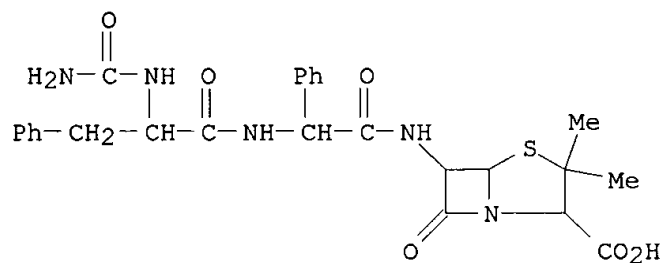
RN 68964-66-9 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



RN 68964-69-2 CAPLUS

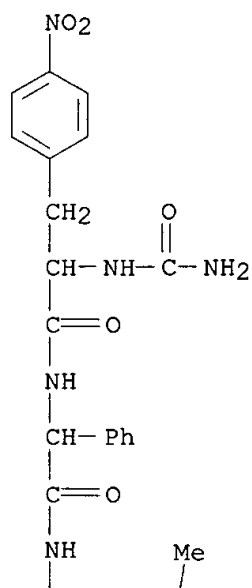
CN Glycinamide, N-(aminocarbonyl)-L-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-L-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



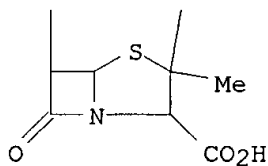
RN 68964-77-2 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-4-nitrophenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)

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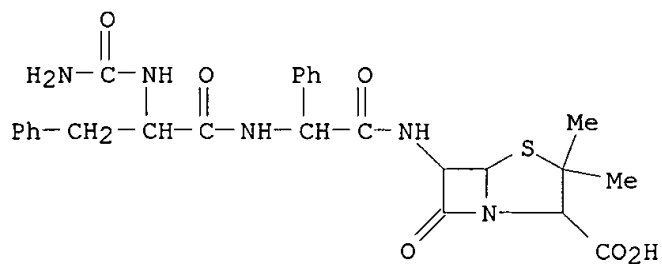


PAGE 2-A



RN 68985-99-9 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-L-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

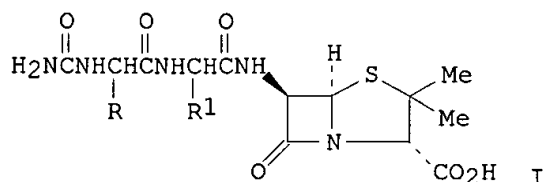


GI

Patel

&lt;5/25/2003&gt;





AB Alkyl, aryl, aralkyl, and heterocyclic substituted 6-[(.alpha.-(.alpha.'-ureidoacylamino)acylamino]penicillanic acids (I) were synthesized by the reaction of appropriate .alpha.-aminopenicillins with either the isobutoxy formic anhydrides or the N-succinimido esters of ureido acids. The effects of the substitutions on the in vitro antibacterial activities of the compds. indicated that size, shape, and stereochem. of a substituent were of greater influence than its lipophilic or electronic properties. Some of the more active derivs. [e.g., I(R = PhCH<sub>2</sub>, R<sub>1</sub> = C<sub>6</sub>H<sub>4</sub>OH-4) [54896-34-3] and I(R = 3-indolylmethyl, R<sub>1</sub> = Ph) [54896-37-6]] were more effective than com. available penicillins.

L4 ANSWER 133 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1978:597534 CAPLUS

DN 89:197534

TI Penicillins

IN Ferres, Harry; Kemmenoe, Adrian Victor; Best, Desmond John

PA Beecham Group Ltd., UK

SO Brit., 7 pp.

CODEN: BRXXAA

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | GB 1509924 | A    | 19780504 | GB 1974-25182   | 19750604 |
|    |            |      |          | GB 1974-25182   | 19750604 |

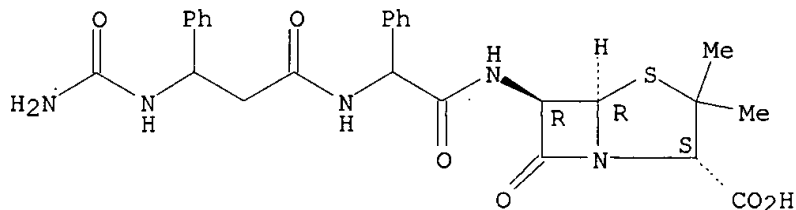
IT **68196-68-9P 68196-69-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(bactericide, prepn. of)

RN 68196-68-9 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[3-[(aminocarbonyl)amino]-1-oxo-3-phenylpropyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

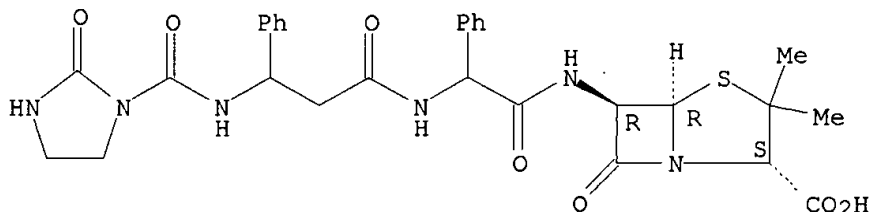
Absolute stereochemistry.



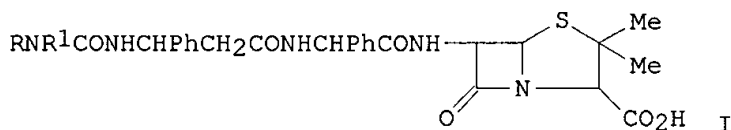
RN 68196-69-0 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 3,3-dimethyl-7-oxo-6-  
 [[[[[1-oxo-3-[(2-oxo-1-imidazolidinyl)carbonyl]amino]-3-  
 phenylpropyl]amino]phenylacetyl]amino]-, [2S-(2.alpha.,5.alpha.,6.beta.)]-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB The prepn. is described of penicillins I (R, R<sup>1</sup> = H, C<sub>1</sub>-6 alkyl, PhCH<sub>2</sub>, C<sub>1</sub>-6 alkanoyl, Ph optionally substituted by 1 or 2 C<sub>1</sub>-6 alkyl groups; NRR<sup>1</sup> = ring), which have broad spectrum antibacterial activity (no data). Thus, I (R = R<sup>1</sup> = H) was prepd. (29.8%) from DL-.beta.-phenyl-.beta.-ureidopropionic acid by sequential treatment with ClCO<sub>2</sub>CH<sub>2</sub>CHMe<sub>2</sub>-Et<sub>3</sub>N (in Me<sub>2</sub>CO, -10.degree., 0.5 h) and aq. D-(.alpha.-aminophenylacetamido)penicillanic acid-Et<sub>3</sub>N (in Me<sub>2</sub>CO, -40.degree. to room temp., 40 min).

L4 ANSWER 134 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1976:121815 CAPLUS

DN 84:121815

TI Penicillins

IN Ferres, Harry

PA Beecham Group Ltd., UK

SO Ger. Offen., 24 pp.

CODEN: GWXXBX

DT Patent

LA German

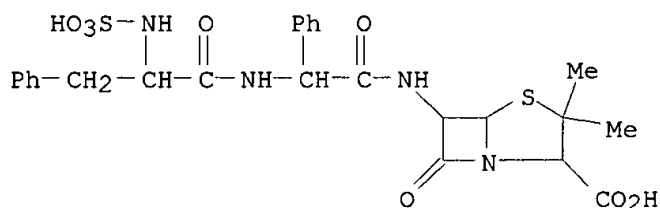
FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | DE 2526924 | A1   | 19760102 | DE 1975-2526924 | 19750616 |
|    |            |      |          | GB 1974-26887   | 19740618 |
|    | GB 1503918 | A    | 19780315 | GB 1974-26887   | 19740618 |
|    | US 3987032 | A    | 19761019 | US 1975-583278  | 19750603 |
|    |            |      |          | GB 1974-26887   | 19740618 |
|    | ZA 7503621 | A    | 19760526 | ZA 1975-3621    | 19750604 |

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| SE 7506835  | A  | 19751219 | AU 1975-82049  | 19750611 |
| NL 7507056  | A  | 19751222 | GB 1974-26887  | 19740618 |
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| BE 830347   | A1 | 19751217 | GB 1974-26887  | 19740618 |
| DK 7502720  | A  | 19751219 | NL 1975-7056   | 19750613 |
| ES 438658   | A1 | 19770616 | GB 1974-26887  | 19740618 |
| CH 611903   | A  | 19790629 | FR 1975-18707  | 19750616 |
| JP 51013792 | A2 | 19760203 | GB 1974-26887  | 19740618 |
|             |    |          | BE 1975-157424 | 19750617 |
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|             |    |          | DK 1975-2720   | 19750617 |
|             |    |          | GB 1974-26887  | 19740618 |
|             |    |          | ES 1975-438658 | 19750617 |
|             |    |          | GB 1974-26887  | 19740618 |
|             |    |          | CH 1975-7876   | 19750617 |
|             |    |          | GB 1974-26887  | 19740618 |
|             |    |          | JP 1975-74234  | 19750618 |
|             |    |          | GB 1974-26887  | 19740618 |

IT **58606-90-9P 58641-47-7P**RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 58606-90-9 CAPLUS

CN Glycinamide, N-sulfo-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, dipotassium salt,  
[2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

● 2 K

RN 58641-47-7 CAPLUS

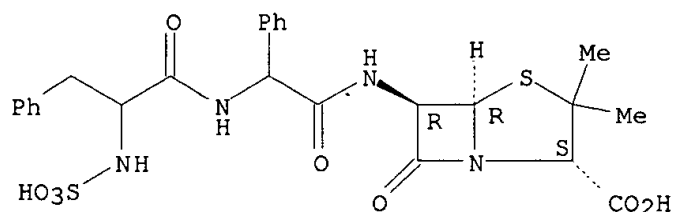
CN Glycinamide, N-sulfophenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]-, compd. with N,N-diethylethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 58641-46-6

CMF C25 H28 N4 O8 S2

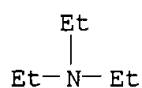
Absolute stereochemistry.



CM 2

CRN 121-44-8

CMF C6 H15 N



IT 18416-41-6

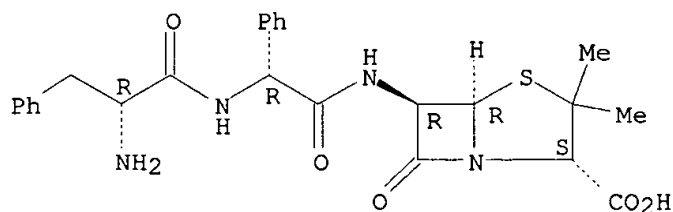
RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with sulfur trioxide trimethylamine complex)

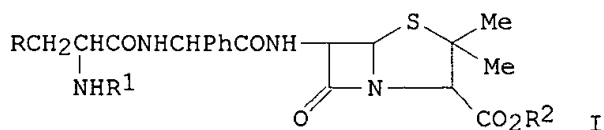
RN 18416-41-6 CAPLUS

CN Glycinamide, D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



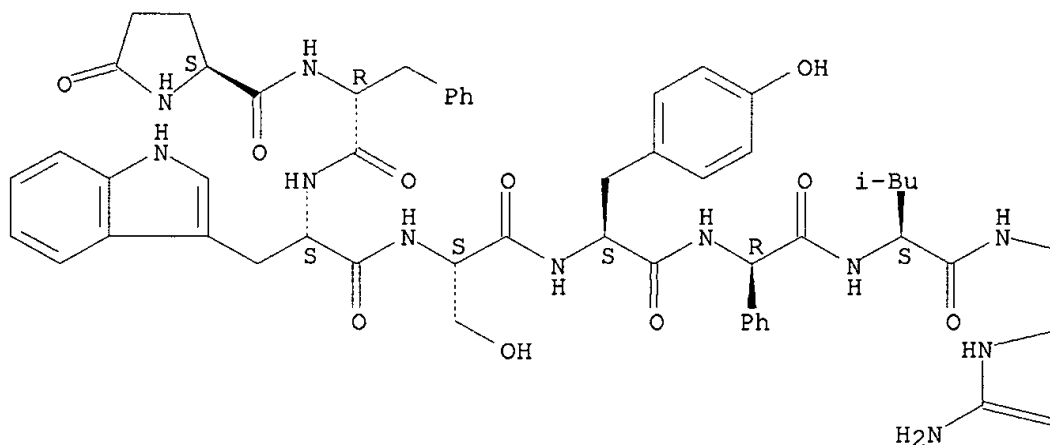
AB Penicillins I (R = Ph, Me, R1 = SO3R2, R2 = K; R = 3-indolyl, MeSCH2, R1 = SO3R2, R3 = Na; R = Ph, R1 = SO3R2, R2 = NHET3) were prepd. by treating I (R1 = H) with SO3-NMe3 and the salt-forming cation.

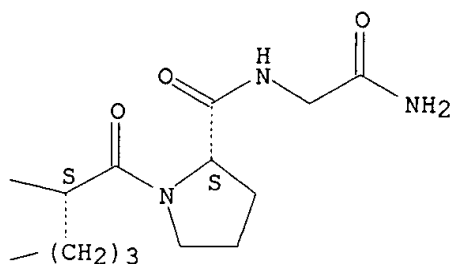
L4 ANSWER 135 OF 148 CAPLUS COPYRIGHT 2003 ACS  
AN 1976:12740 CAPLUS

DN 84:12740  
TI Luteinizing hormone-releasing hormone. Antiovulatory activity of analogs substituted in positions 2 and 6  
AU Beattie, C. W.; Corbin, A.; Foell, T. J.; Garsky, V.; McKinley, W. A.; Rees, R. W. A.; Sarantakis, D.; Yardley, J. P.  
CS Res. Dev. Div., Wyeth Lab., Philadelphia, PA, USA  
SO Journal of Medicinal Chemistry (1975), 18(12), 1247-50  
CODEN: JMCMAR; ISSN: 0022-2623  
DT Journal  
LA English  
IT **56558-32-8P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and contraceptive activity of)  
RN 56558-32-8 CAPLUS  
CN Luteinizing hormone-releasing factor (swine), 2-D-phenylalanine-6-(D-2-phenylglycine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





=NH

AB Ten analogs of LH-releasing hormone [33515-09-2] substituted in position 2 with D-amino acids and at 6 with a .beta.-amino acid or nonasymmetric amino acid were prepd. by solid-phase synthesis and assayed for antiovarulatory activity in rats. One of the most active compds. was [D-p-F-Phe2-D-Ala6]-LH-RH [57383-17-2]. Structure-activity relations were discussed.

L4 ANSWER 136 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1975:606562 CAPLUS

DN 83:206562

TI PyroGlu-His-Trp-Ser-Tyr-D-Pgl-Leu-Arg-Pro-Gly-NH2 and intermediates

IN McKinley, Wayne A.; Sarantakis, Dimitrios

PA American Home Products Corp., USA

SO U.S., 5 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | US 3901872 | A    | 19750826 | US 1974-450909  | 19740313 |
|    |            |      |          | US 1974-450909  | 19740313 |

IT **57356-92-0P**

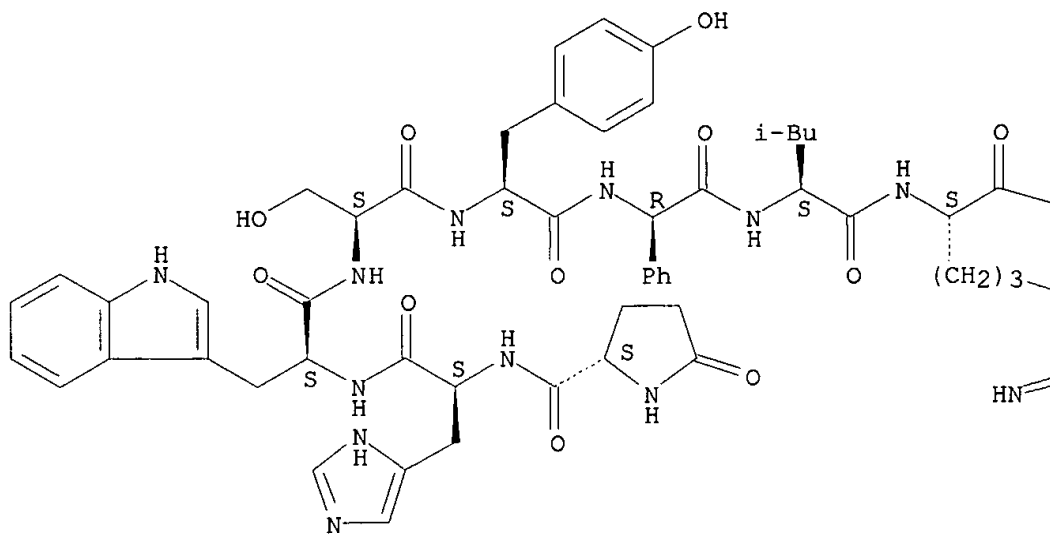
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and LH releasing activity of)

RN 57356-92-0 CAPLUS

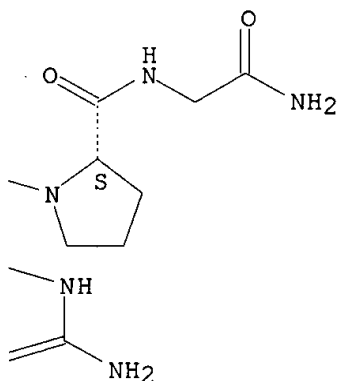
CN Luteinizing hormone-releasing factor (swine), 6-(D-2-phenylglycine)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



AB The title compd., [D-Pgl]6-LRF (Pgl = phenylglycine residue), which stimulated LH relief at a concn. of 0.05 mg/ml and increased the plasma LH level from .apprx.146 to 367 with a dose of 200 mg/rat, was prepd. by solid-phase coupling of the tert-butoxycarbonyl blocked amino acids.

L4 ANSWER 137 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1975:593736 CAPLUS

DN 83:193736

TI PyroGlu-Trp-Ser-Tyr-D-Pgl-Leu-Arg-Pro-Gly-NH<sub>2</sub> (Pgl = phenylglycine) and intermediates

IN McKinley, Wayne A.; Sarantakis, Dimitrios

PA American Home Products Corp., USA

SO U.S., 5 pp.

CODEN: USXXAM

DT Patent  
LA English  
FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | US 3892723 | A    | 19750701 | US 1974-439490  | 19740204 |
|    |            |      |          | US 1974-439490  | 19740204 |

IT **57225-54-4P**

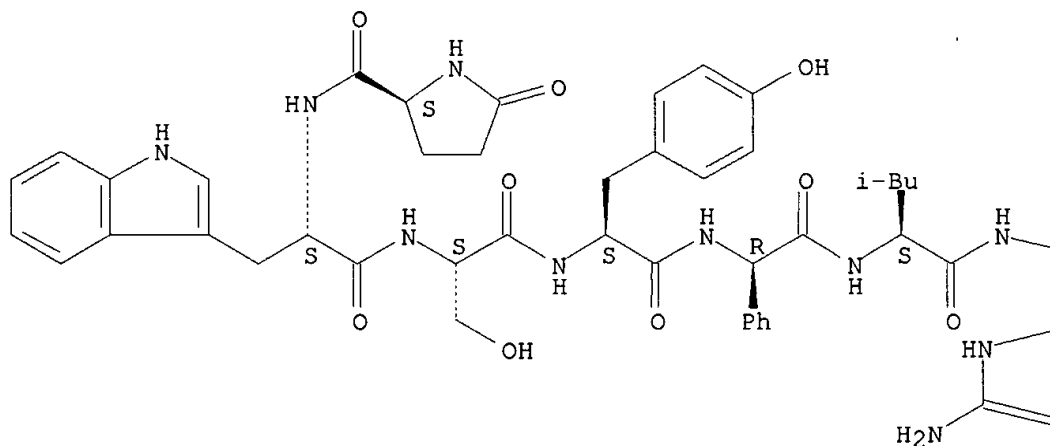
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and ovulation inhibiting activity of)

RN 57225-54-4 CAPLUS

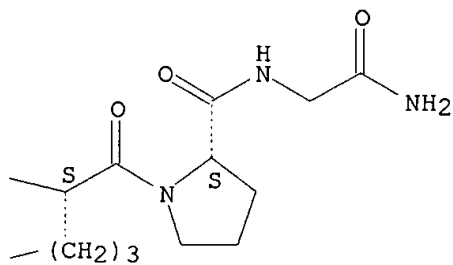
CN Luteinizing hormone-releasing factor (swine), 2-de-L-histidine-6-(D-2-phenylglycine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



=NH



AB The title compd., I, was prepd. by solid phase synthesis on a benzhydrylamine hydrochloride resin and removed with anhyd. liq. HF. I achieved 40% ovulation inhibition in rats at a dose of .apprx.24 mg/kg.

L4 ANSWER 138 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1975:497942 CAPLUS

DN 83:97942

TI Pyro-Glu-D-Phe-Trp-Ser-Tyr-D-Pgl-Leu-Arg-Pro-Gly-NH2 and intermediates

IN McKinley, Wayne A.; Sarantakis, Dimitrios

PA American Home Products Corp., USA

SO U.S., 5 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|-------------|------|----------|-----------------|----------|
| PI | US 3886135  | A    | 19750527 | US 1974-459513  | 19740410 |
|    | GB 1473020  | A    | 19770511 | GB 1975-14281   | 19750408 |
|    |             |      |          | US 1974-459513  | 19740410 |
|    | DE 2515495  | A1   | 19751030 | DE 1975-2515495 | 19750409 |
|    |             |      |          | US 1974-459513  | 19740410 |
|    | ZA 7502270  | A    | 19761124 | ZA 1975-2270    | 19750409 |
|    |             |      |          | US 1974-459513  | 19740410 |
|    | CA 1052773  | A1   | 19790417 | CA 1975-224216  | 19750409 |
|    |             |      |          | US 1974-459513  | 19740410 |
|    | BE 827793   | A1   | 19751010 | BE 1975-155284  | 19750410 |
|    |             |      |          | US 1974-459513  | 19740410 |
|    | NL 7504296  | A    | 19751014 | NL 1975-4296    | 19750410 |
|    |             |      |          | US 1974-459513  | 19740410 |
|    | FR 2267114  | A1   | 19751107 | FR 1975-11217   | 19750410 |
|    | FR 2267114  | B1   | 19781222 |                 |          |
|    |             |      |          | US 1974-459513  | 19740410 |
|    | JP 50154240 | A2   | 19751212 | JP 1975-44160   | 19750410 |
|    |             |      |          | US 1974-459513  | 19740410 |
|    | AU 7580019  | A1   | 19761014 | AU 1975-80019   | 19750410 |
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|    |             |      |          | GB 1974-45657   | 19741022 |
|    | IN 142254   | A    | 19770618 | IN 1975-CA1962  | 19751010 |
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|    |             |      |          | GB 1974-45657   | 19741022 |

IT 56558-32-8P

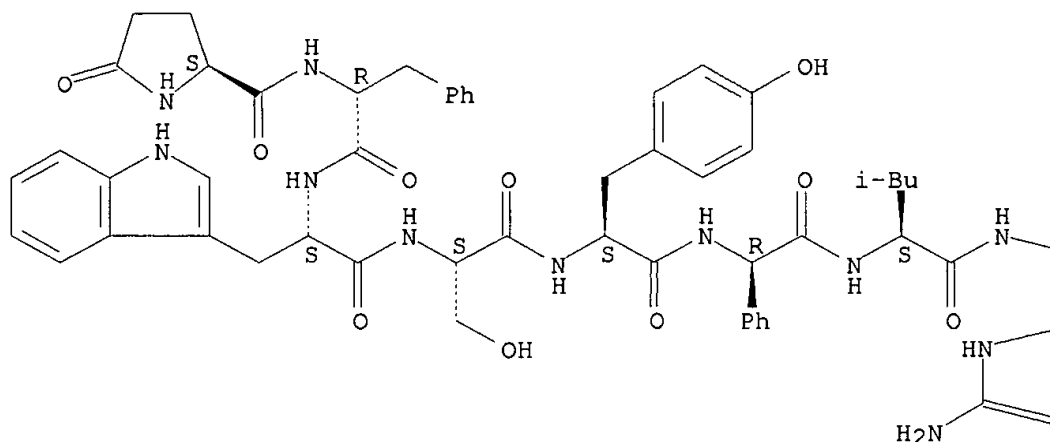
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and ovulation inhibiting activity of)

RN 56558-32-8 CAPLUS

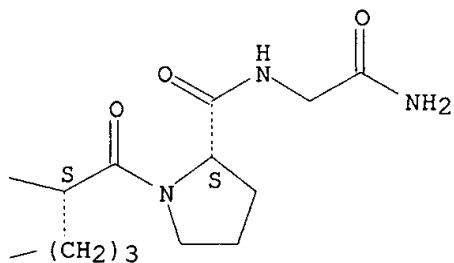
CN Luteinizing hormone-releasing factor (swine), 2-D-phenylalanine-6-(D-2-phenylglycine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



=NH

AB The title compd. (Pgl = phenylglycine residue), effective at inhibiting ovulation in rats at 24 mg/kg s.c., was prepd. by stepwise condensation of the tert-butoxycarbonyl blocked amino acids on a benzhydrylamine resin followed by deblocking and resin release with liq. HF.

L4 ANSWER 139 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1975:410895 CAPLUS  
 DN 83:10895  
 TI Nonapeptideamide derivatives  
 IN Fujino, Masahiko; Fukuda, Tsunehiko; Shinagawa, Susumu  
 PA Takeda Chemical Industries, Ltd., Japan  
 SO Ger. Offen., 54 pp.  
 CODEN: GWXXBX  
 DT Patent  
 LA German  
 FAN.CNT 2

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|-------------|------|----------|-----------------|----------|
| PI | DE 2446005  | A1   | 19750403 | DE 1974-2446005 | 19740926 |
|    | DE 2446005  | C2   | 19820318 |                 |          |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    | JP 50059370 | A2   | 19750522 | JP 1973-109951  | 19730929 |
|    | JP 50121277 | A2   | 19750923 | JP 1974-27442   | 19740308 |
|    | JP 57026506 | B4   | 19820604 |                 |          |
|    | AU 7473694  | A1   | 19760401 | AU 1974-73694   | 19740925 |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    | AT 347054   | B    | 19781211 | AT 1974-7726    | 19740925 |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    | SE 7412140  | A    | 19750401 | SE 1974-12140   | 19740926 |
|    | SE 420717   | B    | 19811026 |                 |          |
|    | SE 420717   | C    | 19820204 |                 |          |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    | ZA 7406118  | A    | 19751126 | ZA 1974-6118    | 19740926 |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    | GB 1434694  | A    | 19760505 | GB 1974-41882   | 19740926 |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    | CH 603559   | A    | 19780831 | CH 1974-13047   | 19740926 |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    | BE 820451   | A1   | 19750327 | BE 1974-148990  | 19740927 |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    | NL 7412837  | A    | 19750402 | NL 1974-12837   | 19740927 |
|    | NL 179289   | B    | 19860317 |                 |          |
|    | NL 179289   | C    | 19860818 |                 |          |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    | FR 2245375  | A1   | 19750425 | FR 1974-32580   | 19740927 |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    | DK 7405103  | A    | 19750526 | DK 1974-5103    | 19740927 |
|    | DK 148305   | B    | 19850603 |                 |          |
|    | DK 148305   | C    | 19851202 |                 |          |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    | HU 173783   | P    | 19790828 | HU 1974-TA1323  | 19740927 |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    | ES 430495   | A1   | 19770116 | ES 1974-430495  | 19740928 |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    | FI 7402847  | A    | 19750330 | FI 1974-2847    | 19740930 |
|    | FI 61028    | B    | 19820129 |                 |          |
|    | FI 61028    | C    | 19820510 |                 |          |
|    |             |      |          | JP 1973-109951  | 19730929 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    | NO 7403538  | A    | 19750402 | NO 1974-3538    | 19740930 |
|    | NO 143218   | B    | 19800922 |                 |          |
|    | NO 143218   | C    | 19810102 |                 |          |

US 4008209 A 19770215

JP 58055137 B4 19831208

PATENT FAMILY INFORMATION:

FAN 1976:5401

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|-------------|------|----------|-----------------|----------|
| PI | DE 2509783  | A1   | 19750911 | DE 1975-2509783 | 19750306 |
|    | DE 2509783  | C2   | 19830217 |                 |          |
|    | JP 50121277 | A2   | 19750923 | JP 1974-27442   | 19740308 |
|    | JP 57026506 | B4   | 19820604 | JP 1974-27442   | 19740308 |
|    | AT 348693   | B    | 19790226 | AT 1975-1380    | 19750224 |
|    | AU 7578594  | A1   | 19760826 | JP 1974-27442   | 19740308 |
|    | ZA 7501306  | A    | 19760128 | AU 1975-78594   | 19750226 |
|    | CA 1072953  | A1   | 19800304 | JP 1974-27442   | 19740308 |
|    | NL 7502564  | A    | 19750910 | ZA 1975-1306    | 19750303 |
|    | NL 181658   | B    | 19870504 | JP 1974-27442   | 19740308 |
|    | NL 181658   | C    | 19871001 | CA 1975-221126  | 19750303 |
|    | US 3972859  | A    | 19760803 | JP 1974-27442   | 19740308 |
|    | CS 186284   | P    | 19781130 | US 1975-555126  | 19750304 |
|    | SE 7502520  | A    | 19750909 | JP 1974-27442   | 19740308 |
|    | SE 420718   | B    | 19811026 | CS 1975-1485    | 19750305 |
|    | SE 420718   | C    | 19820204 | JP 1974-27442   | 19740308 |
|    | FR 2262995  | A1   | 19751003 | SE 1975-2520    | 19750306 |
|    | BE 826430   | A1   | 19750908 | JP 1974-27442   | 19740308 |
|    | NO 7500763  | A    | 19750909 | FR 1975-7065    | 19750306 |
|    | NO 145691   | B    | 19820201 | JP 1974-27442   | 19740308 |
|    | NO 145691   | C    | 19820512 | BE 1975-154128  | 19750307 |
|    | DK 7500927  | A    | 19750909 | JP 1974-27442   | 19740308 |
|    | DK 149862   | B    | 19861013 | NO 1975-763     | 19750307 |
|    | DK 149862   | C    | 19870615 | JP 1974-27442   | 19740308 |
|    | ES 435405   | A1   | 19761201 | DK 1975-927     | 19750307 |
|    | GB 1498048  | A    | 19780118 | JP 1974-27442   | 19740308 |
|    | HU 174077   | P    | 19791028 | ES 1975-435405  | 19750307 |
|    | CH 615661   | A    | 19800215 | JP 1974-27442   | 19740308 |
|    |             |      |          | GB 1975-9539    | 19750307 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    |             |      |          | HU 1975-TA1346  | 19750307 |
|    |             |      |          | JP 1974-27442   | 19740308 |
|    |             |      |          | CH 1975-2947    | 19750307 |
|    |             |      |          | JP 1974-27442   | 19740308 |

|            |   |          |                |          |
|------------|---|----------|----------------|----------|
| FI 7500682 | A | 19750909 | FI 1975-682    | 19750310 |
| FI 60859   | B | 19811231 |                |          |
| FI 60859   | C | 19820413 |                |          |
|            |   |          | JP 1974-27442  | 19740308 |
| US 4008209 | A | 19770215 | US 1975-595308 | 19750711 |
|            |   |          | JP 1973-109951 | 19730929 |
|            |   |          | JP 1974-27442  | 19740308 |
|            |   |          | US 1974-509357 | 19740924 |

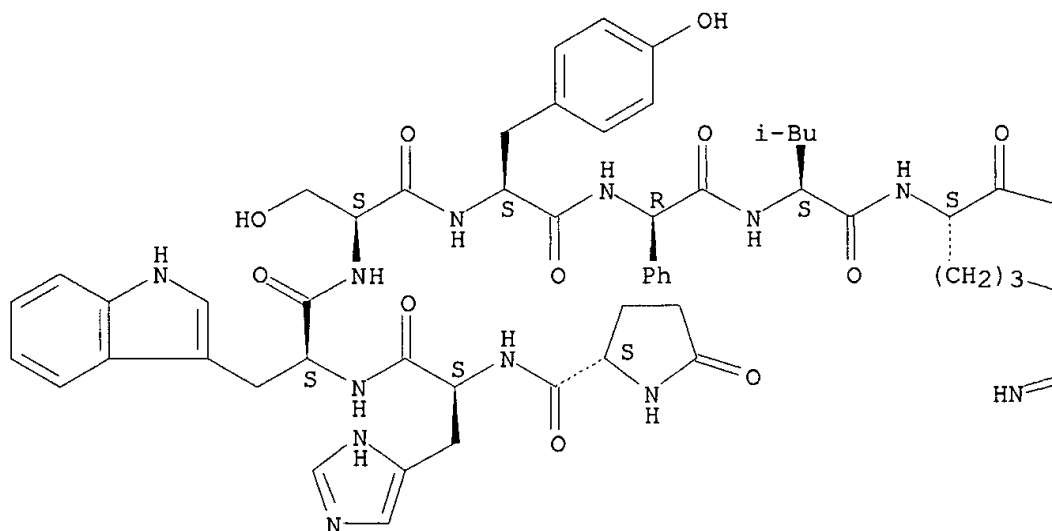
IT **55674-53-8P**RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and LH releasing activity of)

RN 55674-53-8 CAPLUS

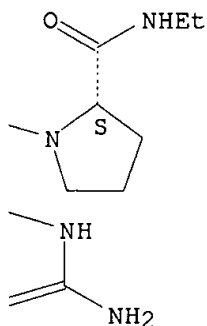
CN Luteinizing hormone-releasing factor (swine), 6-(D-2-phenylglycine)-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



AB Approx. 18 pyroGlu-His-Trp-Ser-X1-X2-X3-Arg-Pro-NHEt (I; X1 = Tyr, Phe; X2 = D-Leu, D-Ile, D-Nle, D-Val, D-Nva, D-Abu, .alpha.-Aibu, D-Phe, D-Phg, D-Ser, D-Tyr, D-Met; X3 = Leu, Ile, Nle; R = Et, Me2CH, Pr; Abu = .alpha.-aminobutyric acid, .alpha.-Aibu = .alpha.-aminoisobutyric acid, Phg = .alpha.-phenylglycine residues) with LH releasing hormone activity 5-60 times greater than found in nature at 2ng-2.mu.g, were prepd. by fragment coupling methods. Thus, N-benzyloxycarbonyl-D-leucine was coupled with Leu-Arg(NO2)-Pro-NHEt followed by coupling with pyroGlu-His-Trp-Ser-Tyr to give I (X1 = Tyr, X2 = D-Leu, X3 = Leu, R = Et).

L4 ANSWER 140 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1975:86286 CAPLUS

DN 82:86286

TI Penicillin derivatives

IN Ferres, Harry; Kemmenoe, Adrian V.; Best, Desmond J.

PA Beecham Group Ltd.

SO Ger. Offen., 81 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | DE 2421030 | A1   | 19741121 | DE 1974-2421030 | 19740430 |
|    |            |      |          | GB 1973-21203   | 19730504 |
|    | GB 1479267 | A    | 19770713 | GB 1973-21203   | 19730504 |
|    | FI 58778   | B    | 19801231 | FI 1974-1265    | 19740424 |
|    | FI 58778   | C    | 19810410 |                 |          |
|    |            |      |          | GB 1973-21203   | 19730504 |
|    | SU 668606  | D    | 19790615 | SU 1974-2026174 | 19740430 |
|    |            |      |          | GB 1973-21203   | 19730504 |
|    | FR 2227858 | A1   | 19741129 | FR 1974-15192   | 19740502 |
|    |            |      |          | GB 1973-21203   | 19730504 |
|    | ZA 7402788 | A    | 19750528 | ZA 1974-2788    | 19740502 |
|    |            |      |          | GB 1973-21203   | 19730504 |
|    | AT 7403643 | A    | 19751015 | AT 1974-3643    | 19740502 |
|    | AT 330957  | B    | 19760726 |                 |          |
|    |            |      |          | GB 1973-21203   | 19730504 |

|             |    |          |                |          |
|-------------|----|----------|----------------|----------|
| AU 7468534  | A1 | 19751106 | AU 1974-68534  | 19740502 |
| BE 814559   | A1 | 19741104 | GB 1973-21203  | 19730504 |
| NL 7406024  | A  | 19741106 | BE 1974-143931 | 19740503 |
| US 3923788  | A  | 19751202 | GB 1973-21203  | 19730504 |
| ES 425945   | A1 | 19761216 | NL 1974-6024   | 19740503 |
| HU 169830   | P  | 19770228 | GB 1973-21203  | 19730504 |
| CH 603663   | A  | 19780831 | US 1974-466814 | 19740503 |
| CS 197231   | P  | 19800430 | GB 1973-21203  | 19730504 |
| RO 67060    | P  | 19821026 | ES 1974-425945 | 19740503 |
| JP 50040589 | A2 | 19750414 | GB 1973-21203  | 19730504 |
| JP 57056479 | B4 | 19821130 | HU 1974-BE1197 | 19740503 |
| DD 111579   | C  | 19750220 | GB 1973-21203  | 19730504 |
| US 3926960  | A  | 19751216 | CH 1974-6057   | 19740503 |
| US 3962216  | A  | 19760608 | GB 1973-21203  | 19730504 |
| US 3935189  | A  | 19760127 | CS 1974-3212   | 19740503 |
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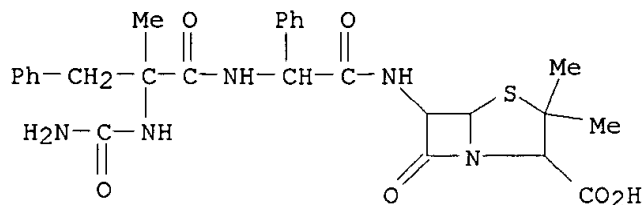
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(prepn. of)

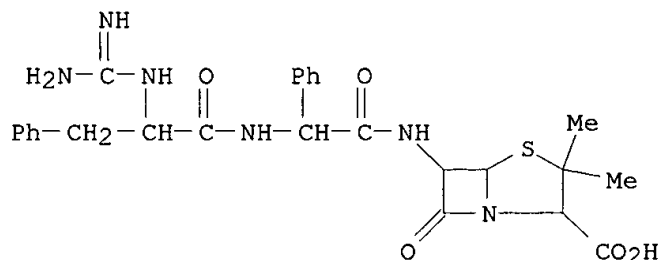
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CN Glycinamide, N-(aminocarbonyl)-.alpha.-methylphenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)



RN 54896-15-0 CAPLUS

CN Glycinamide, N-(aminoiminomethyl)-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, monohydrochloride, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

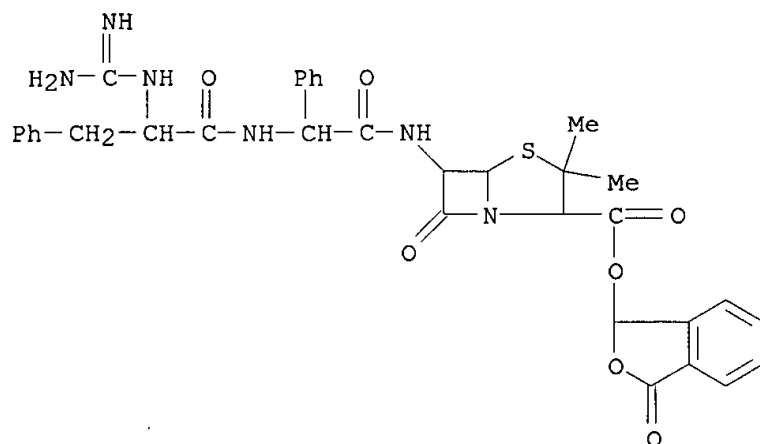


● HCl

RN 54896-16-1 CAPLUS

CN Glycinamide, N-(aminoiminomethyl)-D-phenylalanyl-N-[2-[[[1,3-dihydro-3-oxo-1-isobenzofuranyl]oxy]carbonyl]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-D-2-phenyl-, monohydrochloride, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



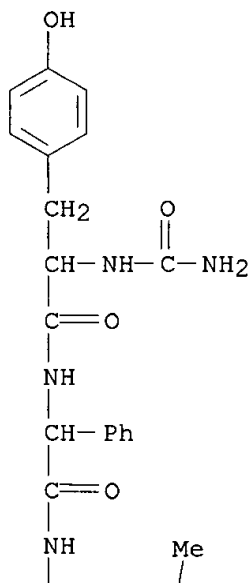


● HCl

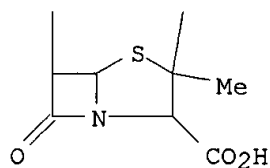
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CN Glycinamide, N-(aminocarbonyl)-D-tyrosyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

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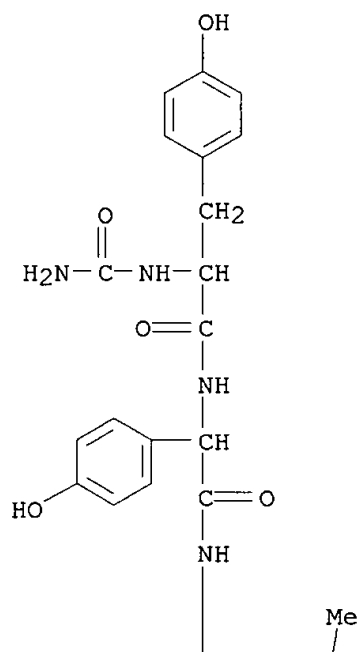
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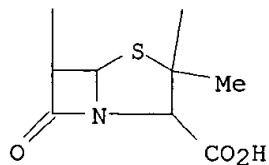
RN 54896-25-2 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-D-tyrosyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-(4-hydroxyphenyl)-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

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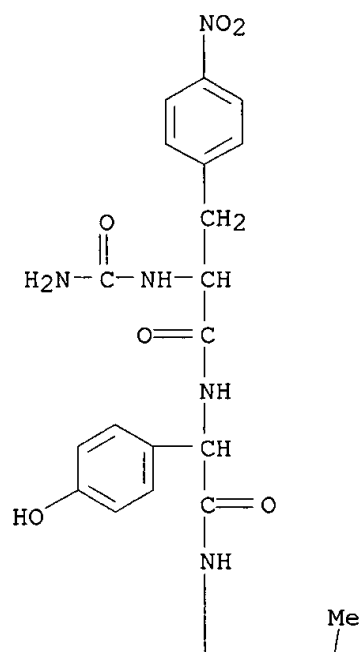
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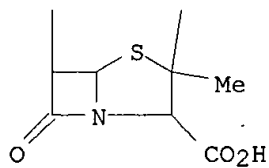
RN 54896-27-4 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-4-nitrophenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-(4-hydroxyphenyl)-, (2R)- (9CI) (CA INDEX NAME)

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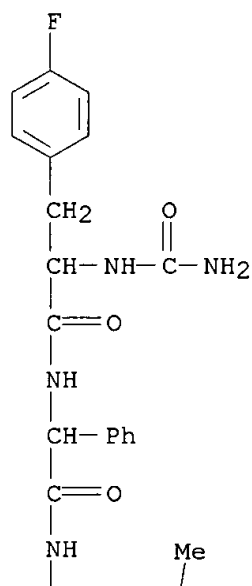


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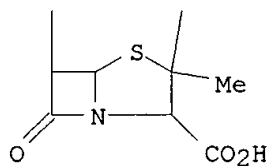
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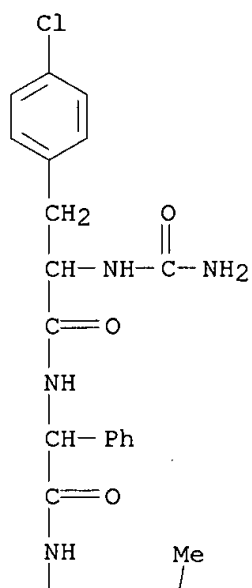
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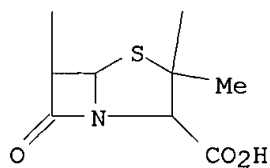
RN 54896-32-1 CAPLUS

CN Glycinamide, N-(aminocarbonyl)-4-chlorophenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)-(9CI) (CA INDEX NAME)

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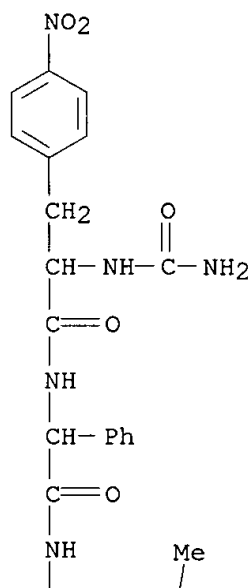


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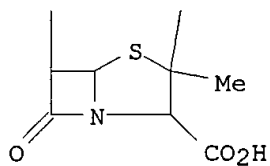


RN 54896-33-2 CAPLUS  
 CN Glycinamide, N-(aminocarbonyl)-4-nitrophenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, monosodium salt, (2R)- (9CI) (CA INDEX NAME)

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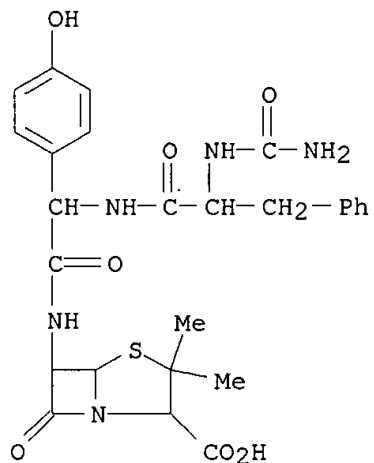


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● Na

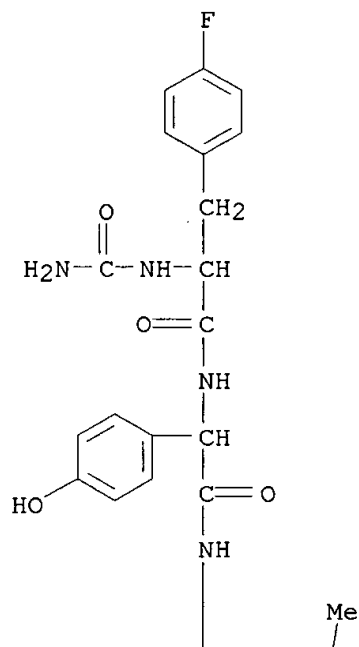
RN 54896-34-3 CAPLUS  
 CN Glycinamide, N-(aminocarbonyl)-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-(4-hydroxyphenyl)-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



RN 54896-35-4 CAPLUS

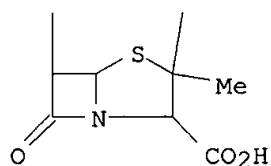
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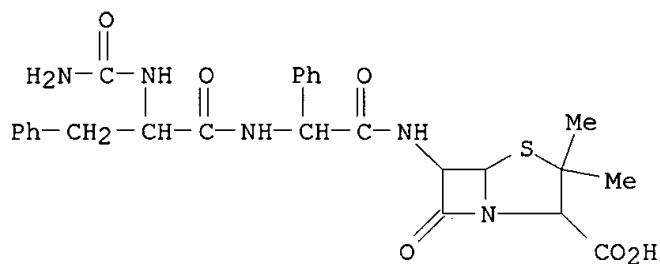


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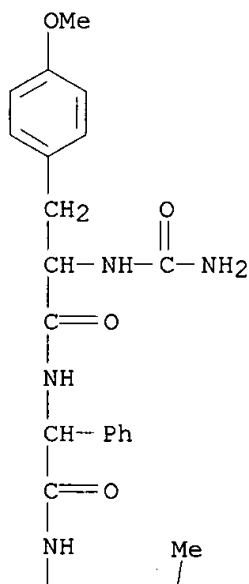
CN Glycinamide, N-(aminocarbonyl)phenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI)  
(CA INDEX NAME)



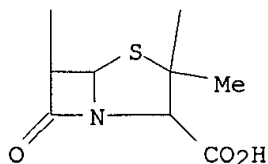
RN 54896-47-8 CAPLUS

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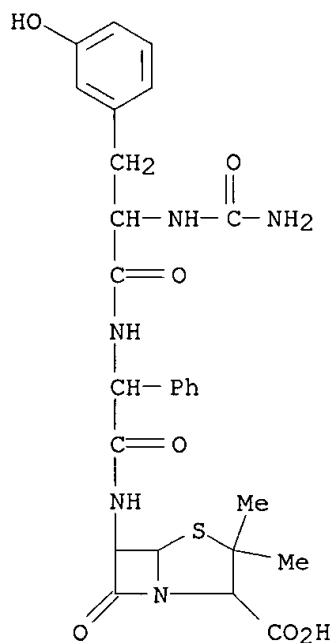


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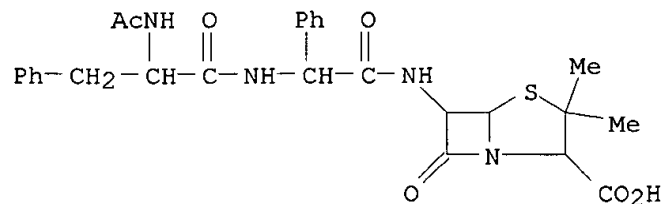
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CN Glycinamide, N-(aminocarbonyl)-3-hydroxyphenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)



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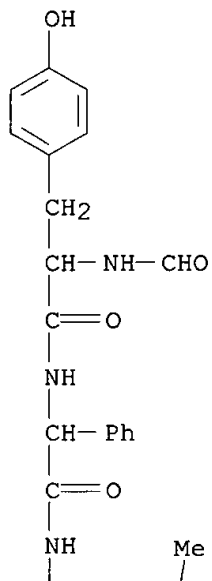
CN Glycinamide, N-acetylphenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)



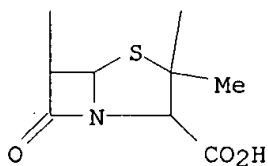
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CN Glycinamide, N-formyltyrosyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)

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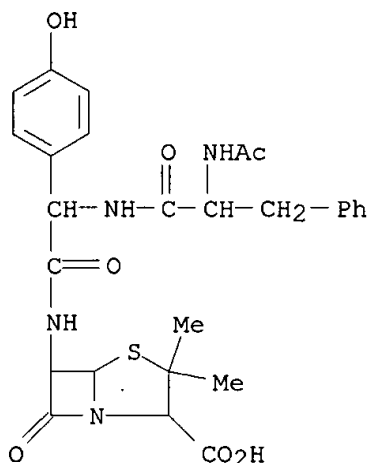


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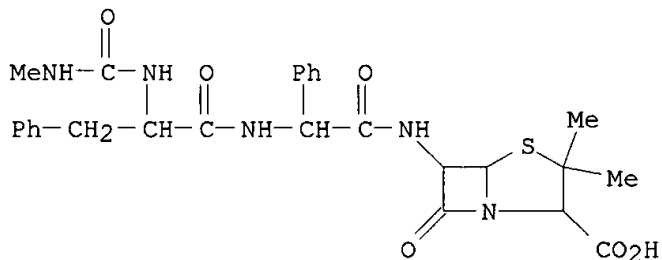
RN 54896-82-1 CAPLUS

CN Glycinamide, N-acetylphenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-(4-hydroxyphenyl)-, (2R)- (9CI) (CA INDEX NAME)



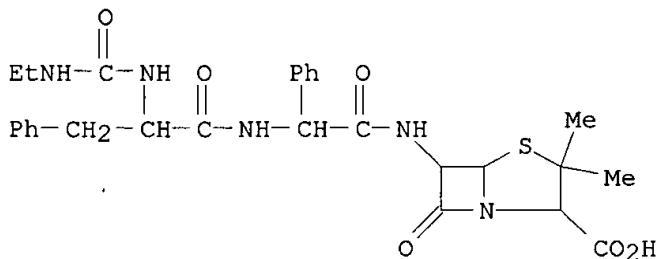
RN 54896-84-3 CAPLUS

CN Glycinamide, N-[(methylamino)carbonyl]phenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)-(9CI) (CA INDEX NAME)



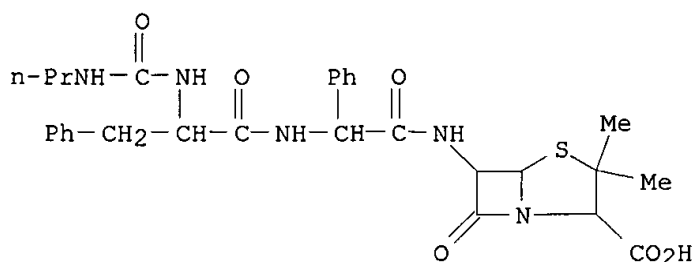
RN 54896-85-4 CAPLUS

CN Glycinamide, N-[(ethylamino)carbonyl]phenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)-(9CI) (CA INDEX NAME)



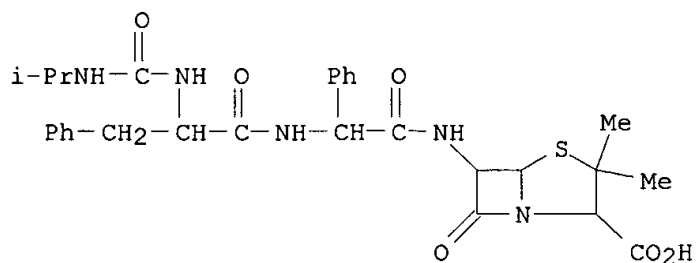
RN 54896-86-5 CAPLUS

CN Glycinamide, N-[(propylamino)carbonyl]-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



RN 54896-87-6 CAPLUS

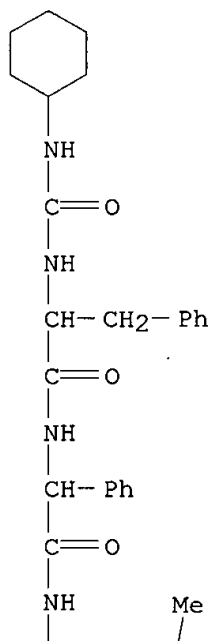
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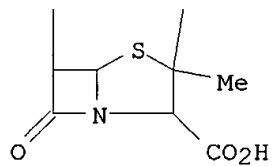
RN 54896-88-7 CAPLUS

CN Glycinamide, N-[(cyclohexylamino)carbonyl]-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, monopotassium salt, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

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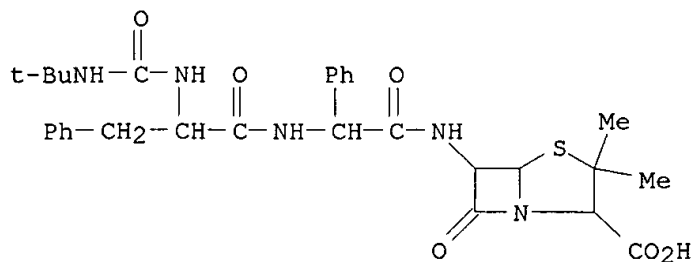


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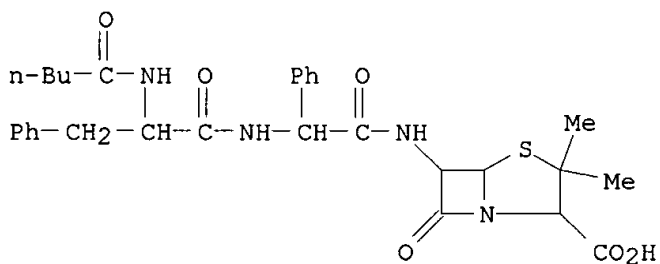
RN 54896-89-8 CAPLUS  
 CN Glycinamide, N-[[[(1,1-dimethylethyl)amino]carbonyl]phenylalanyl-N-  
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● K

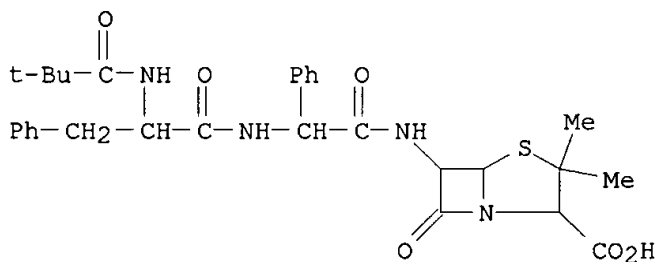
RN 54896-90-1 CAPLUS

CN Glycinamide, N-(1-oxopentyl)-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



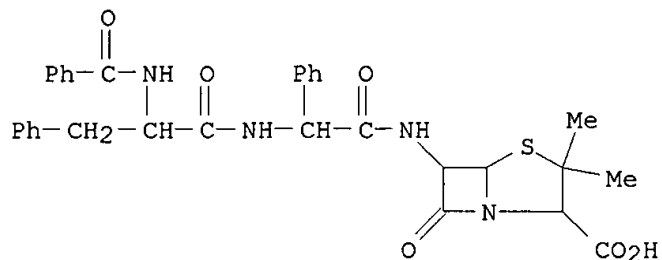
RN 54896-91-2 CAPLUS

CN Glycinamide, N-(2,2-dimethyl-1-oxopropyl)-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



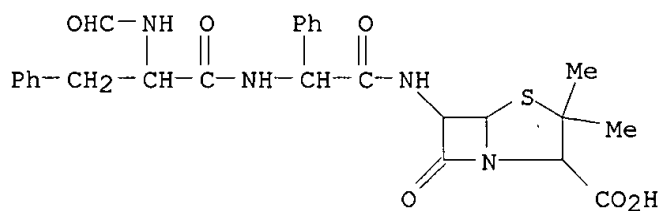
RN 54896-92-3 CAPLUS

CN Glycinamide, N-benzoylphenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)



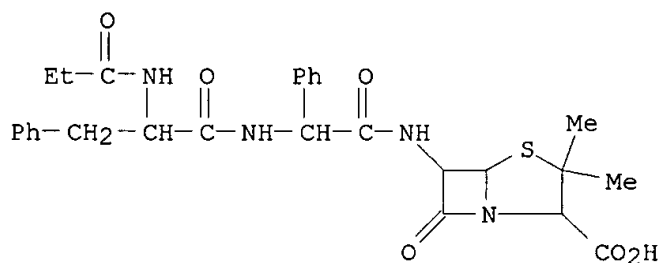
RN 54896-93-4 CAPLUS

CN Glycinamide, N-formylphenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)



RN 54896-94-5 CAPLUS

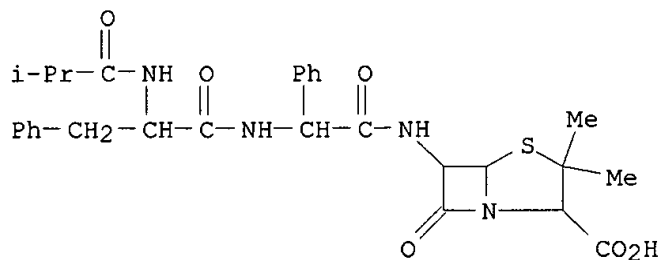
CN Glycinamide, N-(1-oxopropyl)-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



RN 54896-95-6 CAPLUS

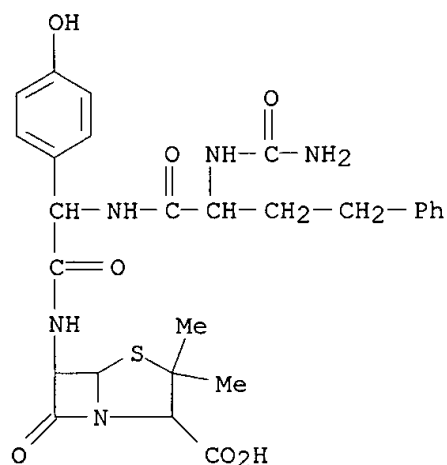
CN Glycinamide, N-(2-methyl-1-oxopropyl)-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)





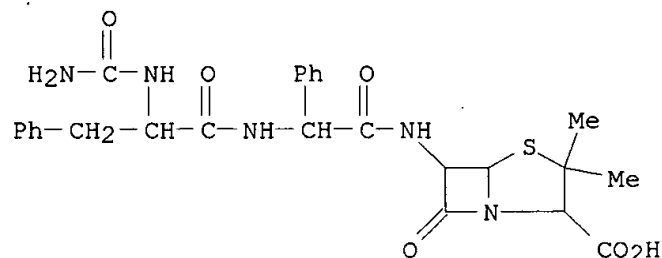
RN 54942-90-4 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[2-(aminocarbonyl)amino]-1-oxo-4-phenylbutyl]amino] (4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-, stereoisomer (9CI) (CA INDEX NAME)



RN 54984-13-3 CAPLUS

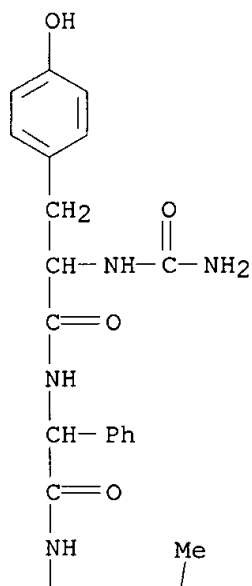
CN Glycinamide, N-(aminocarbonyl)-L-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



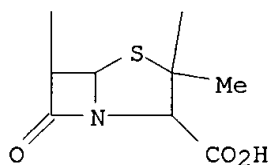
RN 54984-14-4 CAPLUS

CN Glycinamide, N-(aminocarbonyl)tyrosyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)

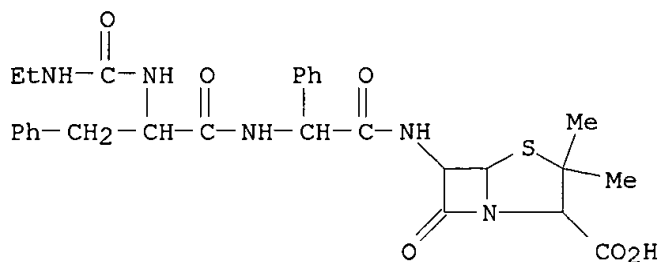
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PAGE 2-A



RN 54984-15-5 CAPLUS  
 CN Glycinamide, N-[(ethylamino)carbonyl]-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-,  
 monopotassium salt, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX  
 NAME)



● K

GI For diagram(s), see printed CA Issue.

AB Sixty-five penicillins I [R = Ph, p-HO-C<sub>6</sub>H<sub>4</sub>, 3-thienyl, 2-thienyl, cyclopropyl, benzyl; R<sub>1</sub> = p-R<sub>4</sub>C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub> (R<sub>4</sub> = HO, O<sub>2</sub>N, Cl, F, H, MeO), MeS(CH<sub>2</sub>)<sub>2</sub>, Me<sub>2</sub>CHCH<sub>2</sub>, Ph(CH<sub>2</sub>)<sub>2</sub>, indol-3-ylmethyl, H<sub>2</sub>NCO(CH<sub>2</sub>)<sub>2</sub>, PhCH<sub>2</sub>OCH<sub>2</sub>, Me, MeOCH<sub>2</sub>, 2-thienylmethyl, m-HOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, Me(CH<sub>2</sub>)<sub>5</sub>, Me(CH<sub>2</sub>)<sub>3</sub>, Me<sub>2</sub>CH, 1,4-cyclohexadien-1-ylmethyl; R<sub>2</sub> = CONH<sub>2</sub>, NCHO, Ac, CONHMe, COBu, COCMe<sub>3</sub>, C<sup>OPh</sup>, COEt, COCHMe<sub>2</sub>, C(:NH)NH<sub>2</sub>.HCl, CONHEt, CONHPr, 3-cyclohexylcarbonyl, CONHCMe<sub>3</sub>; R<sub>3</sub> = H, Me; .alpha. = D, DL, L; R<sub>5</sub> = H, Na, NH<sub>4</sub><sup>+</sup>, 3-phthalidyl, K], with min. inhibitory concns. against .beta.-lactamase-producing Staphylococcus strains 5-12.5 .gamma./ml, were prepd. A) A soln. of D-.alpha.-guanidino-.beta.-phenylpropionic acid (II) and HCl in DMF was added to 3-phthalidyl D-.alpha.-aminophenylacetamidopenicillanate at 0.degree. and the mixt. stirred 0.5 hr at 0.degree. and 1.5 hr at room temp. to give I [R = Ph, R<sub>1</sub> = PhCH<sub>2</sub>, R<sub>2</sub> = NHC(:NH)NH<sub>2</sub>.HCl, R<sub>3</sub> = H, R<sub>5</sub> = 3-phthalidyl, .alpha. = D]. B) A ureido or substituted-ureido acid in acetone was treated with Et<sub>3</sub>N (or N-methylmorpholine) and ClCO<sub>2</sub>CH<sub>2</sub>CHMe<sub>2</sub> (or ClCO<sub>2</sub>Et) at -10.degree. and after 30 min, cooled to -40.degree. and added to D-.alpha.-aminophenyl(p-hydroxyphenyl, 2- or 3-thienyl, 1,4-cyclohexadien-1-yl, cyclopropyl)acetamido-penicillanic acid-3H<sub>2</sub>O and Et<sub>3</sub>N in aq. acetone. D-.alpha.-Aminovaleramido- and D-.alpha.-aminopropionamidopenicillanic acid were also used. C) D-.alpha.-Aminophenylacetamidopenicillanic acid (III) in CH<sub>2</sub>Cl<sub>2</sub> was treated with NEt<sub>3</sub>, then Me<sub>3</sub>SiCl, the mixt. heated 1 hr under N, cooled, and treated with II in DMF previously treated with CH<sub>2</sub>Cl<sub>2</sub> and dicyclohexylcarbodiimide (DCC), and the whole stirred at 0.degree. 1 hr to give I (R = Ph, R<sub>1</sub> = PhCH<sub>2</sub>, R<sub>2</sub> = NHC(:NH)NH<sub>2</sub>, R<sub>3</sub> = H, R<sub>5</sub> = H, .alpha. = D). D) DCC was added at 0.degree. to N-substituted amino acid in acetone and kept overnight. III.3H<sub>2</sub>O was dissolved in acetone, H<sub>2</sub>O, and Et<sub>3</sub>N. The hydroxysuccinimide ester was hydrolyzed to give the free acid. DMF, acetone-DMF, or (MeOCH<sub>2</sub>)<sub>2</sub> were also used as solvents.

L4 ANSWER 141 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1973:147610 CAPLUS

DN 78:147610

TI Thiamphenicol phenylalaninate

IN Saiga, Akisuke; Yamanaka, Motosuke; Sato, Takashi

PA Eisai Co., Ltd.

SO Jpn. Kokai Tokkyo Koho, 2 pp.

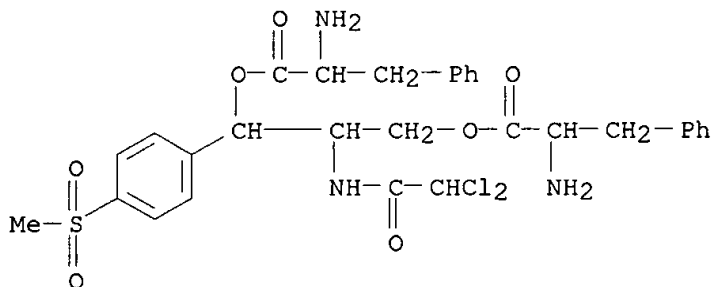
CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

|    | PATENT NO.  | KIND   | DATE     | APPLICATION NO. | DATE     |
|----|---|--------|----------|-----------------|----------|
| PI | JP 48004446   | B4     | 19730120 | JP 1971-27212   | 19710427 |
| IT | <b>41570-11-0P</b>  |        |          |                 |          |
|    | RL: SPN (Synthetic preparation); PREP (Preparation)<br>(prepn. of)  |        |          |                 |          |
| RN | 41570-11-0  | CAPLUS |          |                 |          |
| CN | L-Phenylalanine, 2-[(dichloroacetyl)amino]-1-[4-(methylsulfonyl)phenyl]-1,3-propanediyl ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME) |        |          |                 |          |



AB A soln. of thiamphenicol and  $\text{PhCH}_2\text{CH}(\text{NH}_2)\text{COCl} \cdot \text{HCl}$  (1:2 by mole) in anhyd. dioxane was stirred 7 hr at 13-17.degree. to give 61.2% thiamphenicol phenylalaninate, which was sol. and stable in  $\text{H}_2\text{O}$ .

L4 ANSWER 142 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1972:488521 CAPLUS  
 DN 77:88521  
 TI 7-(D-Mandelamido)cephalosporanic acid derivatives  
 IN Berges, David Alan; Dunn, George Lawrence; Hoover, John R. E.  
 PA Smith Kline and French Laboratories  
 SO Ger. Offen., 54 pp.  
 CODEN: GWXXBX  
 DT Patent  
 LA German  
 FAN.CNT 1

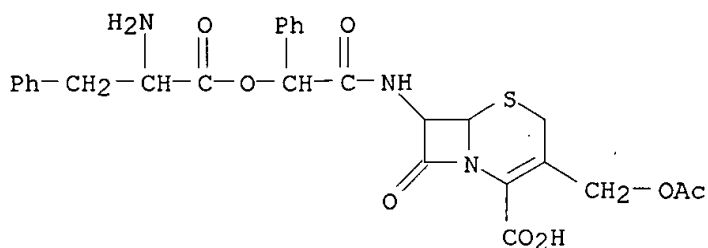
|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | DE 2158330 | A    | 19720608 | DE 1971-2158330 | 19711124 |
|    | US 3701775 | A    | 19721031 | US 1970-92860   | 19701125 |
|    | ZA 7107133 | A    | 19720726 | US 1970-92860   | 19701125 |
|    | CA 960662  | A1   | 19750107 | US 1970-92860   | 19711026 |
|    | BE 775458  | A1   | 19720517 | CA 1971-126096  | 19701125 |
|    | GB 1327510 | A    | 19730822 | US 1970-92860   | 19711117 |
|    | CH 567515  | A    | 19751015 | BE 1971-110605  | 19701125 |
|    | FR 2115363 | A5   | 19720707 | US 1970-92860   | 19711123 |
|    | FR 2115363 | B1   | 19750613 | GB 1971-54335   | 19701125 |
|    | ES 397308  | A1   | 19740516 | US 1970-92860   | 19711123 |
|    |            |      |          | US 1970-92860   | 19701125 |
|    |            |      |          | FR 1971-42022   | 19711124 |
|    |            |      |          | US 1970-92860   | 19701125 |
|    |            |      |          | ES 1971-397308  | 19711124 |

IT 37650-89-8P 37650-90-1P 37651-00-6P  
37651-01-7P

RN 37650-89-8 CAPLUS

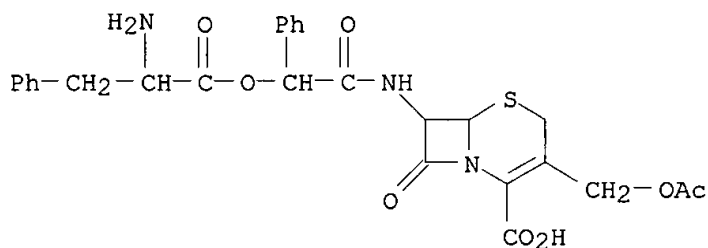
RN 37650-90-1 CAPLUS

RN 37651-00-6 CAPLUS



RN 37651-01-7 CAPLUS

CN L-Phenylalanine, 2-[[3-[(acetyloxy)methyl]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl]amino]-2-oxo-1-phenylethyl ester, [6R-[6.alpha.,7.beta.(R\*)]]- (9CI) (CA INDEX NAME)



AB Fifty-nine title compds. [I, R = e.g., N3CH2CO, H2NCH2CO, Boc-L-methionyl (Boc = Me3CO2C), Boc-D-alanyl, L-methionyl, MeSCH2CO, 2-thenoyl, etc., R1 = e.g., OAc, H, MeO], bactericides, were prepd. via O-acylation of I (R = H) in the presence of N, N -carbonyldiimidazole (II). Thus, II and then I (R = H, R1 = OAc) were added to Boc-methionine in THF, the mixt. was kept 20 hr, and the imidazole salt hydrolyzed to give 50% I (R = Boc-methionyl, R1 = OAc), from which the Boc group was cleaved with CF3CO2H.

L4 ANSWER 143 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1970:67270 CAPLUS

DN 72:67270

TI Water soluble antibiotic chloramphenicol .beta.-phenylalanine ester salts

IN Zumin, Silva T.; Mosna, Sergio

PA Pierrel S.p.A.

SO Brit., 8 pp.

CODEN: BRXXAA

DT Patent

LA English

FAN.CNT 1

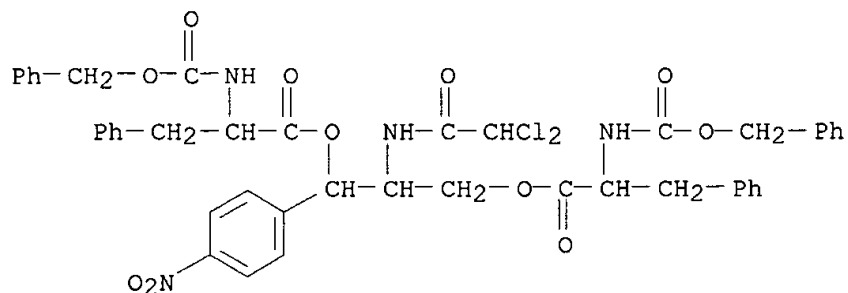
|    | PATENT NO.                                 | KIND | DATE     | APPLICATION NO. | DATE     |
|----|--|------|----------|-----------------|----------|
| PI | GB 1173562                                 |      | 19691210 | GB              | 19660425 |
| IT | <b>25613-59-6P 25613-62-1P 25613-63-2P</b> |      |          |                 |          |
|    | <b>25613-64-3P 25616-21-1P 25616-22-2P</b> |      |          |                 |          |

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 25613-59-6 CAPLUS

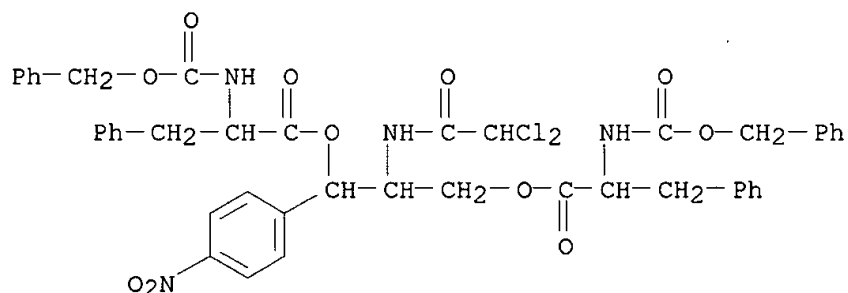
CN Alanine, N-carboxy-3-phenyl-, N-benzyl ester, L-, diester with  
D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-

nitrophenethyl]acetamide (8CI) (CA INDEX NAME)



RN 25613-62-1 CAPLUS

CN Alanine, N-carboxy-3-phenyl-, N-benzyl ester, DL-, diester with  
D-threo-2,2-dichloro-N-[(1S)-1-phenyl-2-oxo-3-phenylpropanamido]-p-  
nitrophenethyl]acetamide (8CI) (CA INDEX NAME)



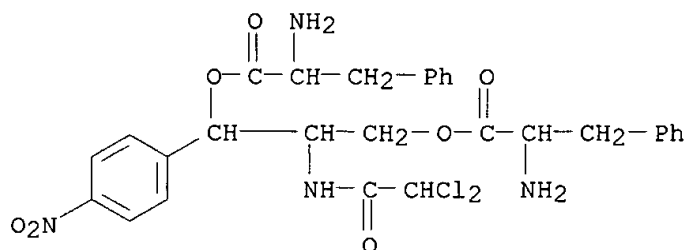
RN 25613-63-2 CAPLUS

CN Alanine, phenyl-, L-, diester with D-threo-2,2-dichloro-N-[(1S)-1-phenyl-2-oxo-3-phenylpropanamido]-p-nitrophenethyl]acetamide, bis(trifluoroacetate)  
(8CI) (CA INDEX NAME)

CM 1

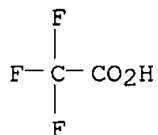
CRN 47832-98-4

CMF C29 H30 Cl2 N4 O7

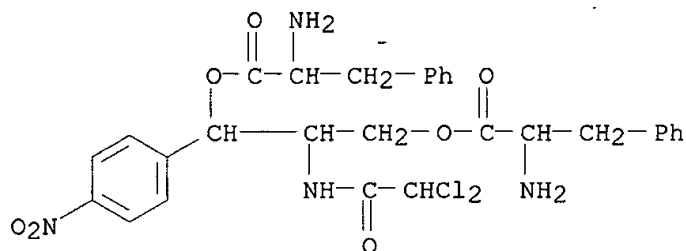


CM 2

CRN 76-05-1  
CMF C2 H F3 O2



RN 25613-64-3 CAPLUS  
CN Alanine, phenyl-, L-, diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide, dihydrochloride (8CI)  
(CA INDEX NAME)

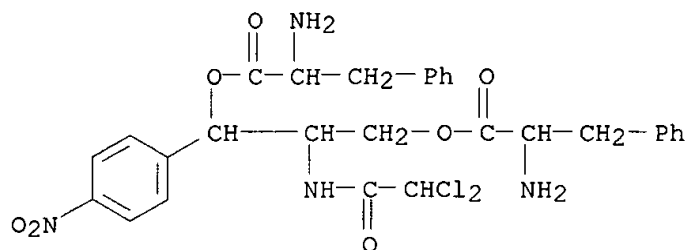


● 2 HCl

RN 25616-21-1 CAPLUS  
CN Alanine, N-acetyl-3-phenyl-, L-, compd. with L-phenylalanine diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide (2:1) (8CI) (CA INDEX NAME)

CM 1

CRN 47832-98-4  
CMF C29 H30 Cl2 N4 O7

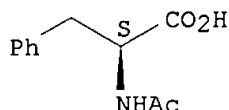


CM 2

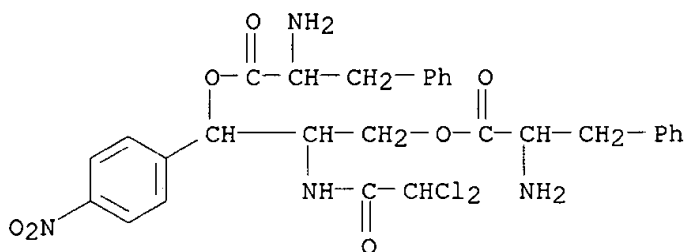


CRN 2018-61-3  
CMF C11 H13 N O3

Absolute stereochemistry. Rotation (+).



RN 25616-22-2 CAPLUS  
CN Alanine, phenyl-, DL-, diester with D-threo-2,2-dichloro-N-[.beta.-hydroxy-.alpha.-(hydroxymethyl)-p-nitrophenethyl]acetamide, dihydrobromide (8CI)  
(CA INDEX NAME)



● 2 HBr

AB Salts of chloramphenicol 1,3-bis(L-.beta.-phenylalaninate) (I) and chloramphenicol 3-L-.beta.-phenylalaninate (II), useful for parenteral administration, with antibiotic activity, were prepd. by reacting D-(-)-threo-1-p-nitrophenyl-2-dichloroacetamido-1,3-propanediol (chloramphenicol) (III) either with N-carbobenzoxy-L-.beta.-phenylalanine (IV) in the presence of dicyclo-hexylcarbodiimide (V) and anhyd. pyridine (VI) or with IV anhydride (VII) in the presence of VI to give chloramphenicol 1,3-bis(N-carbobenzoxy-L-.beta.-phenylalaninate) (VIII) and chloramphenicol 3-(N-carbobenzoxy-L-.beta.-phenylalaninate) (IX), resp., followed by removal of the protecting group(s) by treatment with aq. HBr or anhyd. CF3CO2H. I and II are hydrolyzed in vivo to III and phenylalanine. Thus, addn. of 10.30 g V at 15.degree. to a stirred soln. of 29.93 g IV in 150 ml Me2CO, and the mixt. stirred 3 hr gave 96.5% VII. Racemic N-carbobenzoxy-DL-.beta.-phenylalanine anhydride (X) (93.5%) was prepd. similarly. III (5.82 g) in 10 ml VI was added to 180 ml of an Me2CO soln. of 25.2 g VII and the mixt. stirred 5-6 hr at room temp. and poured on ice-HCl to give, after treatment with 3.5 ml p-H2NC6H4NMe2 (XI) in dry C6H6 to remove excess VII, 90% VIII, m. 95-7.degree.. Racemic chloramphenicol 1,3-bis(N-carbobenzoxy-.beta.-phenylalaninate) (XII) (94%), a yellow oil, was prepd. similarly from X. IV (22.45 g) and 15 ml VI added to a stirred soln. of 9.69 g III in 60 ml HCONMe2, the soln. cooled to -5 to -8.degree., 18.57 g V added slowly, the mixt. stirred 1 hr, kept 3 hr at -5.degree. and poured on a mixt. of 50 ml concd. HCl, 50 ml H2O, and 100 g ice gave a ppt., which was centrifuged off and extd.

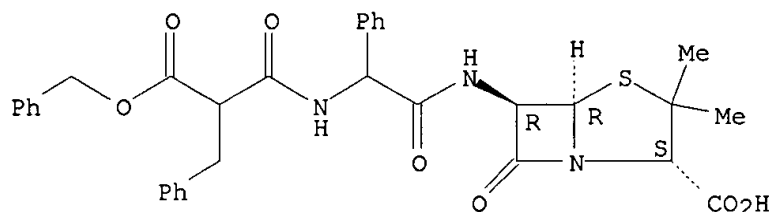
with C<sub>6</sub>H<sub>6</sub>. Treatment of the C<sub>6</sub>H<sub>6</sub> ext. with 3.5 ml XI gave 93% VIII, m. 95-7.degree.. IX, m. 145-7.degree., was prepd. similarly using 19.39 g III, 60 ml HCONMe<sub>2</sub>, 17.96 g IV, 15 ml VI, and 12.38 g V. A mixt. of 17.72 g VIII and 40 ml anhyd. CF<sub>3</sub>CO<sub>2</sub>H refluxed 1 hr in the presence of 8 g resorcinol gave 16.30 g I.CF<sub>3</sub>CO<sub>2</sub>H (XIII). Addn. of XIII to satd. aq. NaHCO<sub>3</sub>, extn. of the free base with CH<sub>2</sub>Cl<sub>2</sub>, and treatment of the ext. with HCl gave I.HCl, m. 220-222.degree. (decompn.). II.HCl, [.alpha.]2D<sub>0</sub> 10.77.degree. (c 2, H<sub>2</sub>O), was prepd. similarly from IX. A soln. of 5 g XII in 60 ml 2.5N HBr in AcOH stirred 10 min at 25 .degree. gave 85% a mixt. of chloramphenicol 1,3-bis(D- and L-.beta.-phenylalaninate-HBr) sepd. by chromatog. XIII (13 g) treated with satd. aq. NaHCO<sub>3</sub>, extn. of the free base with CH<sub>2</sub>Cl<sub>2</sub>, and treatment of the ext. with N-acetyl-L-phenylalanine gave III 1,3-bis(L-.beta.-phenylalaninate N-acetyl-L-phenylalaninate); III 3-(L-.beta.-phenylalaninate N-acetyl-L-phenylalaninate) was prepd. similarly.

L4 ANSWER 144 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1969:524426 CAPLUS  
 DN 71:124426  
 TI Penicillins  
 IN Hardy, Kenneth D.  
 PA Beecham Group Ltd.  
 SO Ger. Offen., 16 pp. Addn. to Ger. Offen. 1545615  
 CODEN: GWXXBX  
 DT Patent  
 LA German  
 FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | DE 1901918 | A    | 19690911 | DE 1969-1901918 | 19690115 |
|    |            |      |          | GB 1968-2968    | 19680119 |
|    | GB 1210472 | A    | 19701028 | GB 1968-2968    | 19680119 |
|    | BE 726979  | A    | 19690716 | BE 1969-726979  | 19690116 |
|    |            |      |          | GB 1968-2968    | 19680119 |
|    | AT 296498  | B    | 19720210 | AT 1969-440     | 19690116 |
|    |            |      |          | GB 1968-2968    | 19680119 |
|    | NL 6900875 | A    | 19690722 | NL 1969-875     | 19690117 |
|    |            |      |          | GB 1968-2968    | 19680119 |
|    | FR 2000429 | A6   | 19690905 | FR 1969-714     | 19690117 |
|    |            |      |          | GB 1968-2968    | 19680119 |
|    | ES 362645  | A2   | 19701201 | ES 1969-362645  | 19690117 |
|    |            |      |          | GB 1968-2968    | 19680119 |
|    | BR 6905659 | A0   | 19730208 | BR 1969-205659  | 19690117 |
|    |            |      |          | GB 1968-2968    | 19680119 |
|    | CH 499548  | A    | 19701130 | CH 1969-499548  | 19690120 |
|    |            |      |          | GB 1968-2968    | 19680119 |
|    | US 3647780 | A    | 19720307 | US 1970-20457   | 19700323 |
|    |            |      |          | GB 1968-2968    | 19680119 |

IT **24121-58-2P 24121-65-1P 24170-67-0P**  
**24199-64-2P 25671-21-0P 26088-51-7P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 24121-58-2 CAPLUS  
 CN Malonamic acid, 2-benzyl-N-[.alpha.-[(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)carbonyl]benzyl]-, 1-benzyl ester,  
 monosodium salt (8CI) (CA INDEX NAME)

Absolute stereochemistry.

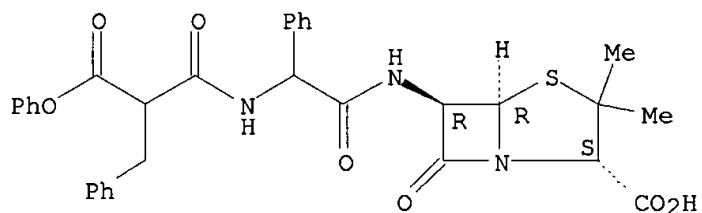


● Na

RN 24121-65-1 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[1,3-dioxo-3-phenoxy-2-(phenylmethyl)propyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

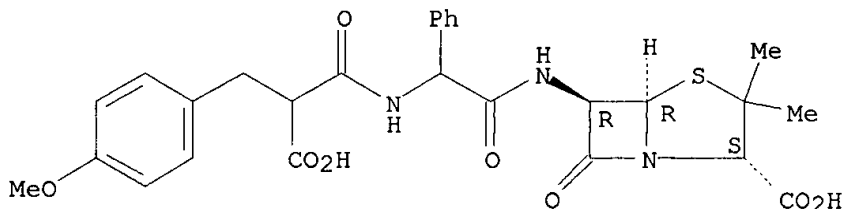
Absolute stereochemistry.



RN 24170-67-0 CAPLUS

CN Malonamic acid, N-[.alpha.-[(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)carbamoyl]benzyl]-2-(p-methoxybenzyl)-, disodium salt (8CI) (CA INDEX NAME)

Absolute stereochemistry.

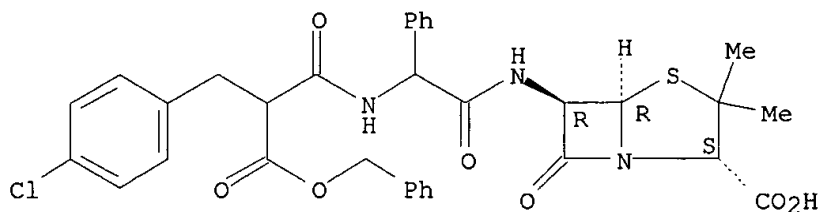


●2 Na

RN 24199-64-2 CAPLUS

CN Malonamic acid, N-[.alpha.-[(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)carbamoyl]benzyl]-2-(p-chlorobenzyl)-, 1-benzyl ester (8CI) (CA INDEX NAME)

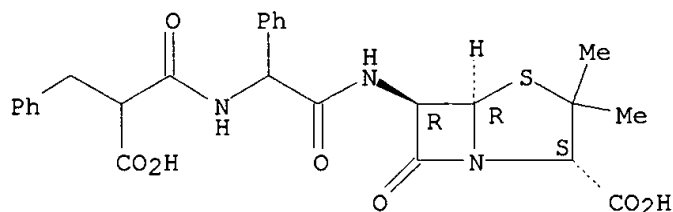
Absolute stereochemistry.



RN 25671-21-0 CAPLUS

CN Malonamic acid, 2-benzyl-N-[.alpha.-[(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)carbamoyl]benzyl]-, disodium salt (8CI) (CA INDEX NAME)

Absolute stereochemistry.

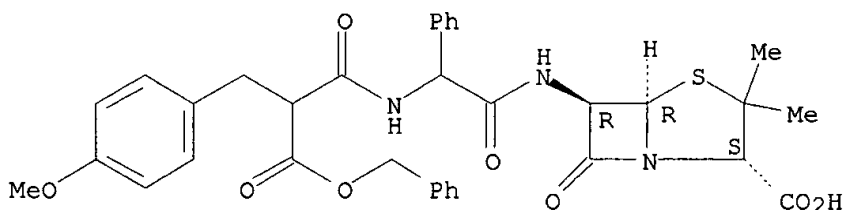


● 2 Na

RN 26088-51-7 CAPLUS

CN Malonamic acid, N-[.alpha.-[(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)carbamoyl]benzyl]-2-(p-methoxybenzyl)-, 1-benzyl ester (8CI) (CA INDEX NAME)

Absolute stereochemistry.



GI For diagram(s), see printed CA Issue.

AB Penicillins (I) are prepd. by treating .alpha.-aminobenzylpenicillin with R1R2C(CO2R)COCl (II). In general, the D-epimers are the most active compds. Thus, a soln. of 9.7 g. PhCH2CH(CO2H)2 in 40 ml. dry Et2O is treated with 5.95 g. SOCl2 and 1 drop HCONMe2 and the mixt. refluxed 3 hrs. to give a residue which is dissolved in 40 ml. Et2O, 5.4 g. PhCH2OH added, the mixt. refluxed 2 hrs., and worked up to give 7 g. PhCH2CH(CO2CH2Ph)CO2H (III), m. 62-4.degree. (C6H6-petroleum ether). A

mixt. of 2.84 g. III and 10 ml. SOCl<sub>2</sub> is heated to 75.degree. to give a residue which is dissolved in 50 ml. dry Me<sub>2</sub>CO, a cold soln. (12.degree.) of 4.03 g. D-.alpha.-aminobenzylpenicillin-3H<sub>2</sub>O 10 ml. N NaOH, 15 ml. N NaHCO<sub>3</sub>, 50 ml. H<sub>2</sub>O, and 25 ml. Me<sub>2</sub>CO added with stirring, the mixt. stirred at room temp. 2 hrs., and worked up to give 5.8 g. Na salt of the D-epimer (IV) of I (R<sub>1</sub> = CH<sub>2</sub>Ph, R<sub>2</sub> = H, R = CH<sub>2</sub>Ph). A soln. of 3 g. IV in 100 ml. H<sub>2</sub>O, added to a prehydrogenated mixt. of 9 g. CaCO<sub>3</sub> (contg. 5% Pd) in 50 ml. H<sub>2</sub>O, is hydrogenated, and worked up to yield 1.5 g. disodium salt of the D-epimer of I (R<sub>1</sub> = CH<sub>2</sub>Ph, R<sub>2</sub> = H, R = Na). Similarly are prepd. the following II and I (R<sub>1</sub>, R<sub>2</sub>, R, % yield of II, m.p. of II and % yield of I given): Ph, Me, CH<sub>2</sub>Ph, 70, 76-8.degree., 90.3; n-Bu, H, CH<sub>2</sub>Ph, 65.5, oil, 90.2; 3-thienyl, H, CH<sub>2</sub>Ph, 38.8, 91-2.degree., 50; PhO, H, CH<sub>2</sub>Ph, 26.6, 89-91.degree., 82.5; PhCH<sub>2</sub>, H, Ph, 37, 59-61.degree., 71.6; Ph, H, o-C<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>CH<sub>2</sub>Ph, 27.4, 106-8.degree., 54.5; p-MeOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, H, CH<sub>2</sub>Ph, 26.4, 58-60.degree., 79.3; p-ClC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, H, CH<sub>2</sub>Ph, 65, 81-2.degree., 49.2; Ph, H, Et, 48.5, 74-6.degree., 56.0; Ph, H, iso-Pr, 62, 64-6.degree., 83.8; 3-thienyl, H, iso-Pr, 53, 82-3.degree., 63.1. Redn. of I (R = CH<sub>2</sub>Ph) yields the following disodium salts of the D-epimer of I (R = Na) (R<sub>1</sub>, R<sub>2</sub> and % yield given): Ph, Me, 78.4; n-Bu, H, 75.2; 3-thienyl, H, 82.2; PhO, H, 62.7; p-MeOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, H, 36.2. Antibacterial data are given.

L4 ANSWER 145 OF 148 CAPLUS COPYRIGHT 2003 ACS  
 AN 1969:68357 CAPLUS  
 DN 70:68357  
 TI Penicillins  
 IN Hatt, Brian W.; Newsome, Peter M.; Smith, Harry  
 PA Beecham Group Ltd.  
 SO S. African, 28 pp.  
 CODEN: SFXXAB  
 DT Patent  
 LA English  
 FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | ZA 6705837 |      | 19680208 | GB              | 19661004 |

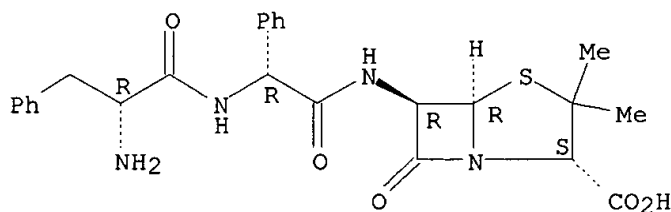
IT **18416-41-6P 21488-12-0P 21488-13-1P**  
**21488-14-2P 21488-15-3P 21488-16-4P**  
**21488-17-5P 21488-18-6P 21488-19-7P**  
**21488-20-0P 21488-22-2P 21488-24-4P**  
**21586-84-5P**

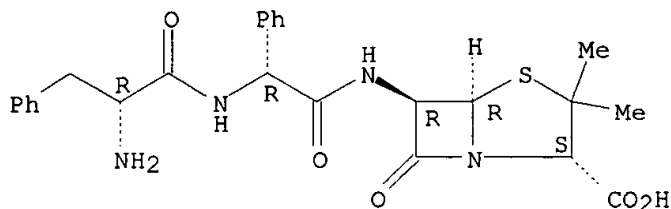
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

RN 18416-41-6 CAPLUS

CN Glycinamide, D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]-(9CI) (CA INDEX NAME)

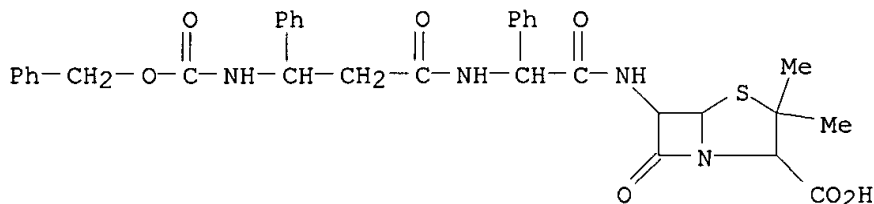
Absolute stereochemistry.





RN 21488-12-0 CAPLUS

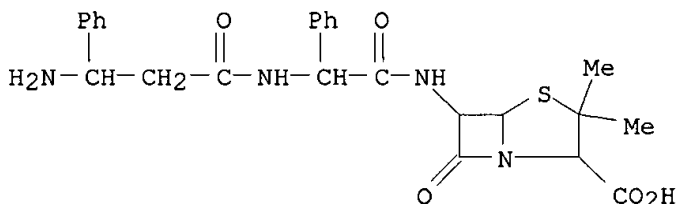
CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[2-[(.beta.-(carboxyamino)hydrocinnamamido]-2-phenylacetamido]-3,3-dimethyl-7-oxo-, N-benzyl ester, monosodium salt (8CI) (CA INDEX NAME)



● Na

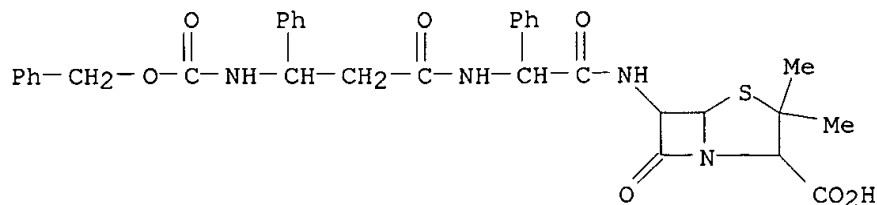
RN 21488-13-1 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[2-[(.beta.-aminohydrocinnamamido)-2-phenylacetamido]-3,3-dimethyl-7-oxo-, stereoisomer (8CI) (CA INDEX NAME)



RN 21488-14-2 CAPLUS

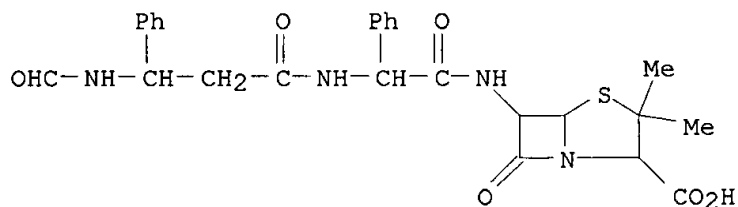
CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[2-[(.beta.-(carboxyamino)hydrocinnamamido)-2-phenylacetamido]-3,3-dimethyl-7-oxo-, N-benzyl ester, monosodium salt (8CI) (CA INDEX NAME)



● Na

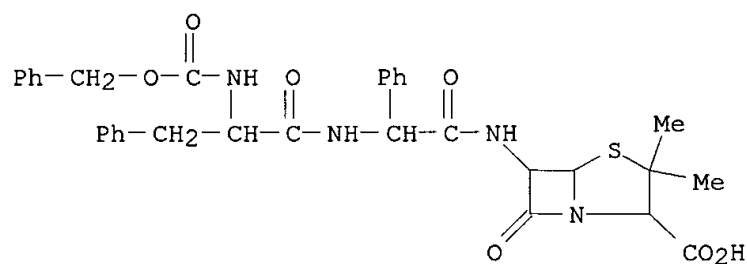
RN 21488-15-3 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[2-(.beta.-formamidohydrocinnamamido)-2-phenylacetamido]-3,3-dimethyl-7-oxo- (8CI)  
(CA INDEX NAME)



RN 21488-16-4 CAPLUS

CN Glycinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, monosodium salt, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

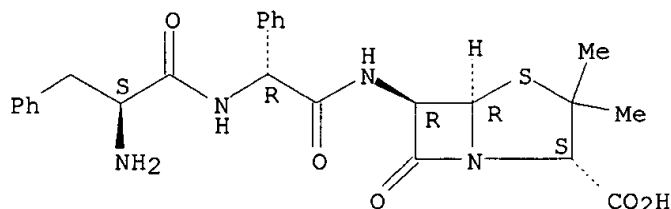


● Na

RN 21488-17-5 CAPLUS

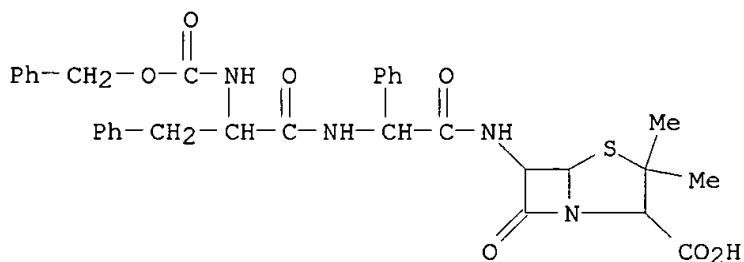
CN Glycinamide, L-phenylalanyl-N-[(2S,5R,6R)-2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl]-2-phenyl-, (2R)- (9CI) (CA INDEX NAME).

Absolute stereochemistry.



RN 21488-18-6 CAPLUS

CN Glycinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-L-2-phenyl-, monosodium salt, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

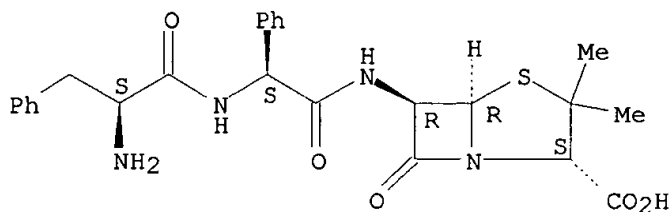


● Na

RN 21488-19-7 CAPLUS

CN Glycinamide, L-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-L-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

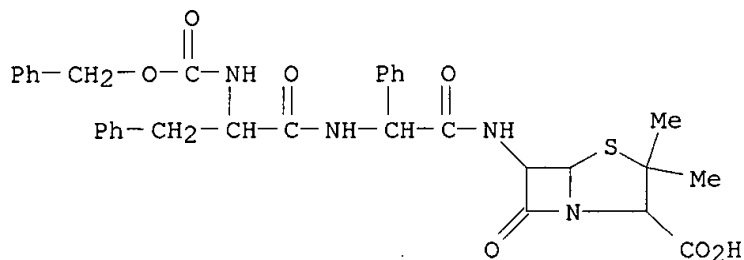
Absolute stereochemistry.



RN 21488-20-0 CAPLUS

CN Glycinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

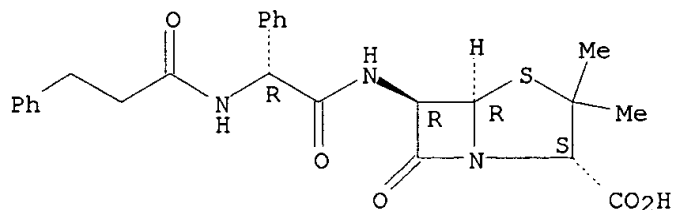




RN 21488-22-2 CAPLUS

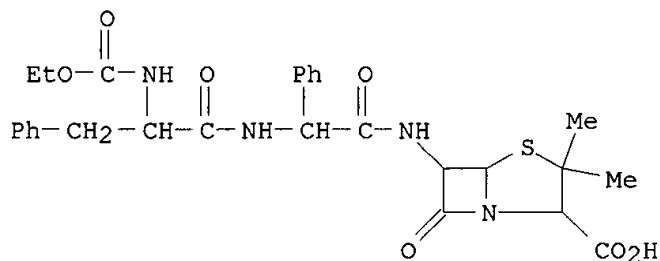
CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 3,3-dimethyl-7-oxo-6-[[[(1-oxo-3-phenylpropyl)amino]phenylacetyl]amino]-, [2S-[2.alpha.,5.alpha.,6.beta.(S\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



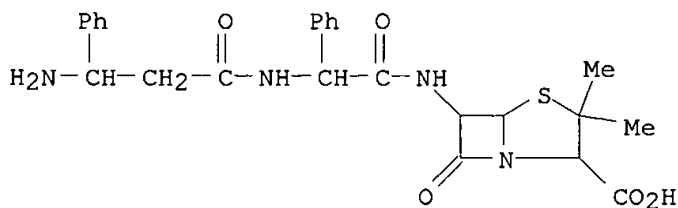
RN 21488-24-4 CAPLUS

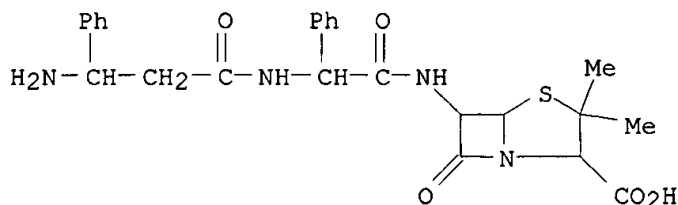
CN Glycinamide, N-(ethoxycarbonyl)-D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)



RN 21586-84-5 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[2-(.beta.-aminohydrocinnamamido)-2-phenylacetamido]-3,3-dimethyl-7-oxo-, stereoisomer (8CI) (CA INDEX NAME)





GI For diagram(s), see printed CA Issue.

AB New penicillins I are prepd. by acylating stereoisomeric 6-.alpha.-phenyl-.alpha.-aminoacetylaminopenicillanic acids with the mixed anhydrides prepd. from the appropriate acid and ClCO<sub>2</sub>Et. Thus, 12.0 g. L-.beta.-(benzyloxycarbonylamino)-.beta.-phenylpropionic acid (L-II) [.alpha.]20D 24.7.degree. (c 1, EtOH), was dissolved in 120 cc. dry tetrahydrofuran contg. 5.6 cc. NEt<sub>3</sub>. The soln. was stirred vigorously and kept at -5.degree. as 3.82 cc. ClCO<sub>2</sub>Et was added. Stirring at -5 to -10.degree. was continued 25 min. The suspension was cooled to -15.degree. and stirred vigorously as a soln. of 16.2 g. of 6-(D-.alpha.-amino-.alpha.-phenylacetamido)penicillanic acid trihydrate (D-III) in 40 cc. H<sub>2</sub>O and 40 cc. tetrahydrofuran (THF) contg. enough NEt<sub>3</sub> to raise the pH to 9.5 was added, the soln. stood 40 min. without cooling, and evapd. at 20.degree. in vacuo, the gelatinous residue was covered with 100 cc. iso-BuCO-Me, stirred vigorously, the ppt. kept at pH 2 by the addn. of 5N HCl, as enough BuOH was added to dissolve the residue, the small residue was filtered, the phases sepd., and the org. phase washed with H<sub>2</sub>O and worked up to give 23.3 g. Na 6-[D-(L-.beta.-benzyloxycarbonylamino) - .beta. - phenylpropionamido - .alpha. - phenylacetamido]penicillanate (D,L-IV) (procedure A). Pd on CaCO<sub>3</sub> (5%) (60 g.) was suspended in 20 cc. H<sub>2</sub>O and shaken with H at room temp. and atm. pressure for 1 hr. A soln. of 10 g. IV in 250 cc. H<sub>2</sub>O was added and the shaking in an atm. of H 45 min. gave 1.5 g. I (R<sub>1</sub> = Ph, Y = NH<sub>2</sub>, X = H, R = Ph) (D,LV) (70% pure) (procedure B). D-III was treated with 12.0 g. DII, [.alpha.]20D -24.8.degree. (c 1, EtOH), to give 22.5 g. D,D-IV (99% pure) using procedure A. D,D-IV (10 g.) was hydrogenated to give 1.2 g. I (R<sub>1</sub> = Ph, Y = NH<sub>2</sub>, X = H, R = Ph) (73% pure) using procedure B. III (2.02 g.) was treated with the reaction product of 0.48 g. ClCO<sub>2</sub>Et 0.97 g. D-.beta.-formamido-.beta.-phenylpropionic acid using procedure A to give 1.3 g. of 6-[D-.alpha.-(D-.beta.-formamido-.beta.-phenylpropionamido)-.alpha.-phenylacetamido]penicillanic acid I (R<sub>1</sub> = Ph, Y = NHCOH, X = H, R = Ph) (85% pure). III (8.06 g.) was treated with the reaction product of 1.91 cc. ClCO<sub>2</sub>Et with 5.98 g. L-.alpha.-benzyloxycarbonylamino-.beta.-phenylpropionic acid (VI) using procedure A to give 9.5 g. Na 6-[D-.alpha.-benzyl-oxycarbonylamino-.beta.-phenylpropionamido)-.alpha.-phenylacetamido]-penicillinate (D,L-VII) (74% pure). D,L-VII was hydrogenated using procedure B to give 0.8 g. 6-[D-.alpha.-(L-.alpha.-amino-.beta.-phenylpropionamido)-.alpha.-phenylacetamido]penicillanic acid I (R<sub>1</sub> = Ph, Y = H, X = NH<sub>2</sub>, R = Ph) (D,L-VIII) (75% pure). L-III (7 g.) was treated with the reaction product of 1.91 cc. ClCO<sub>2</sub>Et with 5.98 g. VI using procedure A to give 10.3 g. L,L-VII (55% pure). L,L-VII (5 g.) was hydrogenated using procedure B to give 2.5 g. I (R<sub>1</sub> = Ph, Y = H, X = NH<sub>2</sub>, R = Ph) (L,L-VIII) (40% pure). D-III (8.06 g.) was treated with 5.98 g. D-VI using procedure A to give 4.6 g. D,D-VII as the free acid, m. 148-9.degree. (MeOH) (decompn.), [.alpha.]2D0 131.5.degree. (c 0.5, MeOH). D,D-VII (2.1 g.) was hydrogenated using procedure B to give 1.5 g. I (R<sub>1</sub> = Ph, Y = H, X = NH<sub>2</sub>, R = Ph) (D,D-VIII) (57% pure). D-III (16 g.) was dissolved in 50 cc. H<sub>2</sub>O

by the dropwise addn. with stirring of 2N NaOH, keeping the pH below 8.5. To this soln., there was added a soln. of 6 cc. .beta.-propionic acid in 40 cc. iso-BuCOMe and the mixt. was stirred vigorously at room temp. 1 hr. to give 8.8 g. 6-[D-.alpha.-(.beta.-phenylpropionamido)-.alpha.-phenylacetamido]penicillanic acid I (R1 = Ph, Y = X = H, R = Ph) (89% pure). A soln. of 4.96 g. D-.alpha.-amino-.beta.-phenylpropionic acid in 100 cc. H2O and 30 cc. 2N NaOH was cooled to 5.degree., 3.3 cc. ClCO2Et was added in one portion and the mixt. stirred without cooling 1 hr. as the pH was kept at 8 by the addn. of 2N NaOH; the soln. was worked up to give 4.3 g. D-.alpha.-(ethoxycarbonylamino)-.beta.-phenylpropionic acid (IX), m. 83-4.degree. (AcOEt-hexane), [.alpha.]20.5D -11.8.degree. (c 2, MeOH). A soln. of 2.37 g. IX in 30 cc. dry Me2CO contg. 1.4 cc. NEt3 was cooled to -5.degree., 0.95 cc. ClCO2Et was added, and the mixt. stirred at -5.degree. for 20 min., cooled to -15.degree., and a soln. of 4.03 g. D-III in 10 cc. H2O, 10 cc. THF, and enough 2N NaOH soln. to give pH 8. The clear soln. was kept 30 min. and worked up to give 3 g. 6-[D-.alpha.-(D-.alpha.-ethoxycarbonylamino-.beta.-phenyl-propionamido)-.alpha.-phenylacetamido]penicillanic acid I (R1 = Ph, Y = H, X = EtOCONH, R = Ph) (88% pure). V was also prepd. as follows: .beta.-amino-L-.beta.-phenylpropionic acid (8.26 g.) was dissolved in 25 cc. 2N NaOH and the clear soln. evapd. to dryness <30.degree. in vacuo over P2O5 to give 9.3 g. of the Na salt. This pulverized Na salt (10.5 g.) was refluxed with 250 cc. EtOH contg. 5.5 cc. Me acetoacetate 15 min., the soln. filtered, kept in a refrigerator overnight, the ppt. filtered, washed, and dried in vacuo over P2O5 to give 9.6 g. Na L-.beta.-(1-methoxycarbonylpro-pen-2-ylamino)-.beta.-phenylpropionate (L-X), m. 260-2.degree. (EtOH) (decompn.). Evapn. of the filtrate gave a second crop (2.6 g.). Dry Me2CO (35 cc.) was cooled to -15.degree. (anhyd. conditions) and 0.96 cc. ClCO2Et was added, followed rapidly by 1 drop of N-methylmorpholine and 2.85 g. X; the temp. was kept at -15.degree. for 25 min. Meanwhile, 4.03 g. III was dissolved in 15 cc. H2O with enough NEt3 to just dissolve the penicillin at pH 8.3. The soln. was cooled to 0-5.degree., 15 cc. Me2CO added, the soln. rapidly cooled to 0.degree. and immediately added to the stirred anhydride. The resulting clear soln. was stirred 20 min. without cooling, concd. in vacuo <25.degree., the viscous residual syrup dild. with 500 cc. distd. H2O, covered with 100 cc. iso-BuCOMe, the vigorously stirred mixt. adjusted to pH 1.5 with 5N HCl, kept at this pH 30 min., the org. phase sepd., the aq. phase re-extd. with iso-BuCOMe, the aq. phase readjusted to pH 4.5 with 40% NaOH soln. and evapd. in vacuo below 30.degree.. When the vol. of the conc. was .apprx.40 cc., the first crop of crystals were filtered, washed, and air-dried at 35.degree. to give 27% V. The filtrate and washings were evapd. <30.degree. to 20 cc. to give a second crop (13%) (procedure C). In the following examples, the 6-(.alpha.-amino-.alpha.-thien-2-ylacetamido)-penicillanic acid was the epimer prepd. from (-)-.alpha.-amino-2-thienylacetic acid (XI), [.alpha.]20D -74.degree. (c 1, H2O). D-.beta.-(Benzyloxy-carbonylamino)-.beta.-phenylpropionic acid was dissolved in 30 cc. dry THF contg. 1.4 cc. NEt3, the soln. was stirred vigorously and kept at -15.degree. as 0.96 cc. ClCO2Et was added in one portion. After keeping at -15.degree. for 20 min., a soln. of 3.55 g. XI, 10 cc. H2O, and enough NEt3 to raise the pH to 9.1 was added to the vigorously stirred soln. at 0.degree.. The resulting soln. was worked up and added dropwise with stirring to 37% Na 2-ethylhexanoate in 4.5 g. iso-BuCOMe dild. with dry Et2O (1:1). The ppt. was filtered off to give 3.8 g. Na [.alpha.-(D-.beta.-benzyloxycarbonylamino-.beta.-phenylpropionamido)-.alpha.-thien-2-ylacetamido]penicillinate. 6-[.alpha.-(L-.beta.-Amino-.beta.-phenylpropionamido)-.alpha.-thien-2-ylacetamido]penicillanic acid I (R1 =

Ph, Y = NH<sub>2</sub>, X = H, R = thienyl) (74% pure) (1.56 g.) was prepd. from 3.55 g. XI using procedure C. D-X, m. 261-2.degree., was prepd. from 8.4 g. D-.beta.-amino-.beta.-phenylpropionate using procedure C and used to prep. 6-[.alpha.-(D-.beta.-amino-.beta.-phenylpropionamido)-.alpha.-thien-2-ylacetamido]penicillanic acid I (R<sub>1</sub> = Ph, Y = NH<sub>2</sub>, X = H, R = thienyl). (97% pure).

L4 ANSWER 146 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1967:520181 CAPLUS

DN 67:120181

TI Amino-acylaminopenicillanic acids

IN Alburn, Harvey E.; Grant, Norman H.

PA American Home Products Corp.

SO U.S., 5 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | US 3340252 |      | 19670905 | US              | 19640407 |

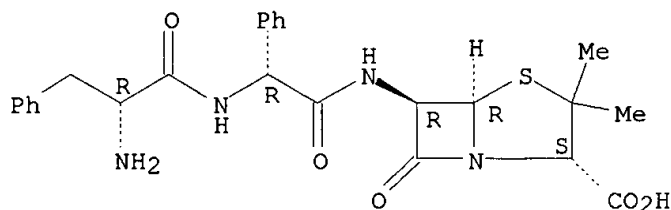
IT **18416-41-6**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(as bactericide)

RN 18416-41-6 CAPLUS

CN Glycinamide, D-phenylalanyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]-(9CI) (CA INDEX NAME)

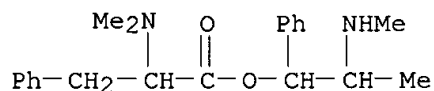
Absolute stereochemistry.



AB Continuation-in-part of U.S. 3,268,513 (CA 65: 16976c). Reaction of 290 mg. 6-(DL-N-methyl-2-aminophenylacetamido)penicillanic acid (I) and 130 mg. isatoic anhydride in 200 ml. H<sub>2</sub>O at 1-2.degree. for 1 hr., maintaining the pH at 6 with 1N NaOH, filtration, and freeze drying gave 6-[DL-2-(o-aminobenzamido)-N-methyl-2-phenylacetamido]-penicillanic acid active against Staphylococcus aureus and Escherichia coli. Similarly prepd. were, using equimolar amts. of the penicillanic acid and an N-carboxy anhydride, the following compds. active against gram-pos. and gram-neg. microorganisms: 6-[DL-2(2-amino-5-nitrobenzamido)-N-methyl-2-phenylacetamido]penicillanic acid, 6-[DL-2-(2-amino-5-methyl-N-methylbenzamido)-2-phenylacetamido]penicillanic acid, 6-[2-(D-2-amino-N-phenylacetamido)acetamido]penicillanic acid, 6-[L-2-(D-2-amino-2-phenylacetamido)-4-methylvaleramido]penicillanic acid, and 6-[2-(D-2-amino-4-methylvaleramido)acetamido]penicillanic acid.

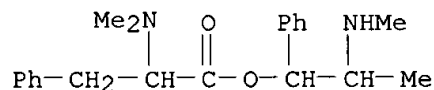
L4 ANSWER 147 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1967:402830 CAPLUS  
 DN 67:2830  
 TI Separation of the organic bases by Craig partition. VII. Acyl migration in the stereoisomeric N-(N,N-dimethylphenylalanyl)ephedrines  
 AU Schoenenberger, Helmut; Fuchsberger, K. D.; Brinkmann, Rolf  
 CS Univ. Munich, Munich, Fed. Rep. Ger.  
 SO Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft (1967), 300(2), 126-35  
 CODEN: APBDAJ; ISSN: 0376-0367  
 DT Journal  
 LA German  
 IT **14355-01-2P 14355-02-3P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 14355-01-2 CAPLUS  
 CN Alanine, N,N-dimethyl-3-phenyl-, ester with (-)-pseudoephedrine, dihydrochloride, L- (8CI) (CA INDEX NAME)



● 2 HCl

RN 14355-02-3 CAPLUS  
 CN Alanine, N,N-dimethyl-3-phenyl-, ester with (-)-pseudoephedrine, dihydrochloride, D- (8CI) (CA INDEX NAME)



● 2 HCl

AB cf. CA 66: 49281u. The compds. studied were N-(L-N,N-dimethylphenylalanyl)-L-ephedrine (I), N-(D-N,N-dimethylphenylalanyl)-L-ephedrine (II), N-(L-N,N-dimethylphenylalanyl)-L-pseudoephedrine (III), and N-(D-N,N-dimethylphenylalanyl)-L-pseudoephedrine (IV). In every case, only the ester of L-pseudoephedrine resulted, even under mild conditions (room temp., acetone-HCl). Complete inversion of the erythro derivs. occurred. In 2N HCl at 80.degree., the ester from I formed quant. in 10 min. while that from III (retention of configuration) required 25 hrs. With II, 5 hrs. and with IV, 22 hrs. were required. The 4 amides pass through either of 2 cyclic intermediates during the migration, L,L-(V) or D,L-pseudooxazolidine (VI). The rates are explained by steric considerations of the mechanism, V resulting from I via inversion and from III with retention, and VI, from II via inversion and IV with retention. Craig partition as described previously (loc. cit.) was used to sep. and det. the reaction products. Twenty-four partition steps using a solvent

mixt. of 0.5M citrate buffer (pH 4/5)-MeOH-CHCl<sub>3</sub> (9:1:10 parts by vol.) were required for sepn. into N- and O-aminoacylphenadrines. The O-(L-N,N-dimethylphenylalanyl)-L-pseudoephedrine m. 170-2.degree., [ $\alpha$ ]<sub>D</sub><sup>20</sup> + 114.degree. (c = 0.0055 g./ml., 5N HCl) and the O-(D-N,N-dimethyl-) ester melts at 174-6.degree., [ $\alpha$ ]<sub>D</sub><sup>20</sup> 48.degree. (c 0.0055 g./ml., 5N HCl).

L4 ANSWER 148 OF 148 CAPLUS COPYRIGHT 2003 ACS

AN 1965:83974 CAPLUS

DN 62:83974

OREF 62:15015a-b

TI .alpha.-Aminobenzylpenicillin

PA Novo Terapeutisk Laboratorium A/S.

SO 3 pp.

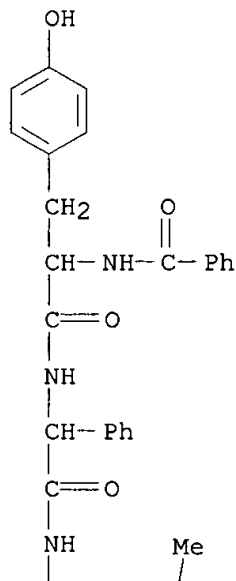
DT Patent

LA Unavailable

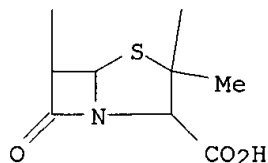
FAN.CNT 1

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|----|--|------|----------|-----------------|----------|
| PI | GB 985688  |      | 19650310 | GB              | 19620828 |
|    | DE 1208302   |      |          | DE              |          |
|    | NL 297126  |      |          | NL              |          |
| IT | <b>2474-95-5</b> , 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[2-(.alpha.-benzamido-p-hydroxyhydrocinnamamido)-2-phenylacetamido]-3,3-dimethyl-7-oxo- (hydrolysis by chymotrypsin) |      |          |                 |          |
| RN | 2474-95-5 CAPLUS   |      |          |                 |          |
| CN | Glycinamide, N-benzoyltyrosyl-N-(2-carboxy-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-6-yl)-D-2-phenyl-, [2S-(2.alpha.,5.alpha.,6.beta.)]-(9CI) (CA INDEX NAME)                         |      |          |                 |          |

PAGE 1-A



PAGE 2-A



AB The title compd. (I) is produced by enzymic cleavage of 6-(N-benzoyl-2-tyrosyl-D( - )-.alpha.-amino-.alpha.-phenylacetamido)penicillanic acid (II) with .alpha.-chymotrypsin (III). The cleavage is selective irresp. of the configuration. Thus, a soln. of 5 mg. III in 0.5 ml. H2O was added to 220 mg. of the Na salt of II dissolved in 30 ml. H2O. The mixt. was left for 2 hrs. at 35.degree. and pH 6.5 to give 95% I, a broad spectrum antibiotic.

=&gt; d cost

COST IN U.S. DOLLARS

| SINCE FILE | TOTAL   |
|------------|---------|
| ENTRY      | SESSION |

CONNECT CHARGES

2.38 3.21

NETWORK CHARGES

0.42 0.60

SEARCH CHARGES

6.56 154.31

DISPLAY CHARGES

731.36 731.36

740.72 889.48

CAPLUS FEE (5%)

37.02 37.02

FULL ESTIMATED COST

777.74 926.50

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

| SINCE FILE | TOTAL   |
|------------|---------|
| ENTRY      | SESSION |

CA SUBSCRIBER PRICE

-96.35 -96.35

IN FILE 'CAPLUS' AT 15:22:02 ON 26 MAY 2003